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1. Macy, I. G.; Kelly, H. J., and Sloan, R. E.: With the Consultation of the Committee on Maternal and Child Feeding of the Food and Nutrition Board, National Research Council: The Composition of Milks, National Academy of Sciences, National Research Council, Publication 254, Revised 1953.

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ARCHIVES OF PEDIATRICS

Albro C. Gaylor, Publisher

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Vol. 77 No. 2

February 1960

CONTENTS

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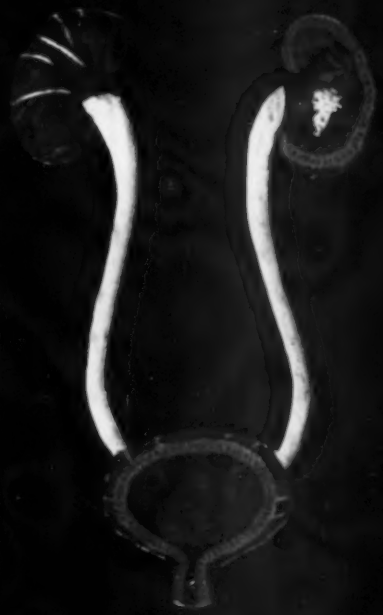

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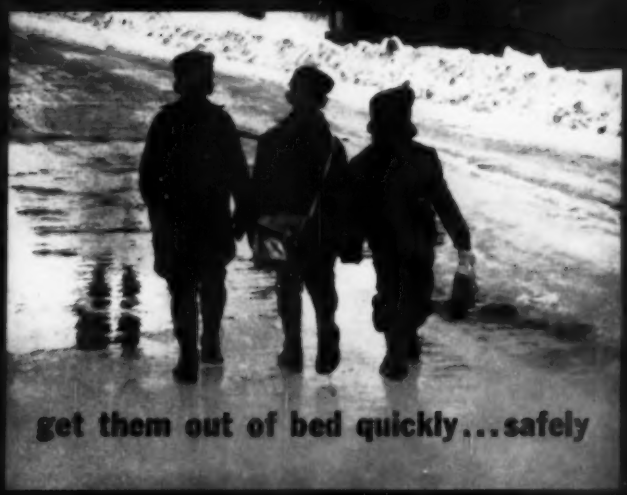

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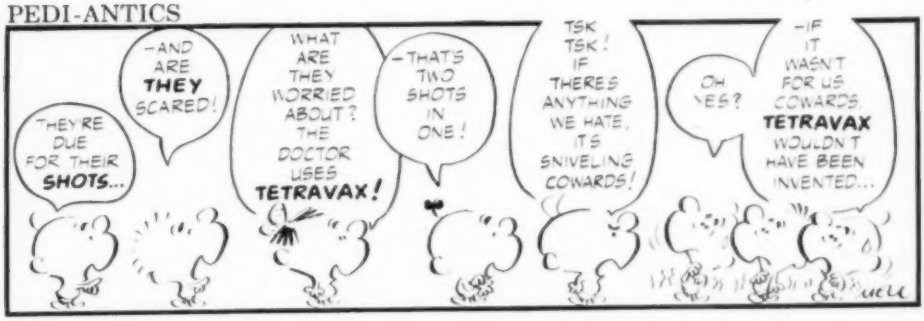

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The Natural History of Dystonia Musculorum Deformans: A Clinical Study*

Angeles Badell Ribera, M.D.** Irving S. Cooper, M.D.***
New York

In 1908, Schwalbe[1] reported the first case of Dystonia Musculorum Deformans and called attention to the appearance of "tonic contractions" and hysterical symptoms. At about the same time, Zienen[2] called the disorder "Torsion-neurose". Oppenheim,[3] in 1911, recognized Dystonia Musculorum Deformans as a disease of the central nervous system and he suggested the alternate name of "dyshasia lordotica progressiva" because of the early appearance of lordosis. He described it as a disorder appearing in children or young adults that had a normal development prior to onset and called attention to the frequent Russian-Jewish ancestry of the patients. The disease itself was described as a motor disorder displaying an alternation between hypotonia and muscle contraction, mostly in the musculature around the pelvic girdle affecting, more or less, the rest of the body. Abnormal movements were intensified by the locomotor functions of standing and walking. The process was recognized as being steadily progressive. The first report in the American literature appeared in 1912 by J. Frenkel,[4] who suggested the name of "tortipelvis" and discussed the analogy with essential torticollis.

* This publication was made possible by a training grant provided by the Office of Vocational Rehabilitation, Department of Health, Education, and Welfare.
Assisted by grants from Sister Elizabeth Kenny Foundation.

** Resident, Department of Neurosurgery, St. Barnabas Hospital.
Resident in Physical Medicine and Rehabilitation, Institute of Physical Medicine and Rehabilitation, New York University Post-Graduate Medical School.

*** Professor of Research Surgery, New York University-Bellevue Medical Center.
Director, Division of Neuromuscular Diseases New York University Post-Graduate School of Medicine.
Director, Department of Neurosurgery, St. Barnabas Hospital.

Over the years it was disputed whether Dystonia Musculorum Deformans was a separate entity or only a variation of other motor disorders. The points of dissension were the difficulty of clinically differentiating it from athetosis and certain forms of chorea, and mainly, the fact that the disease could not be correlated with definite pathology of the brain. For some, it seemed to be a syndrome present in various diseases and, thus, dystonic symptoms were described following encephalitis of different types[5,6] and even after cerebrovascular accidents. For others, there was no such entity as Dystonia Musculorum Deformans and it was instead considered a variation of athetosis called "athetosis with dystonia."[7]

Herz,[8] in 1940, reviewed the literature and found that although many of the cases presented as Dystonia Musculorum Deformans were in fact other diseases, most cases belonged to a typical syndrome and he suggested that the diagnosis of Dystonia Musculorum Deformans should be made only when "together with dystonic movements and dystonic postures there is a gradual development without recognizable etiological factors at the onset". He classified cases of Dystonia Musculorum Deformans into three types, (early, juvenile, and late) of which the most frequent was the juvenile type with onset from five to fifteen years of age. Most authors, starting with Oppenheim, had stressed that the disease always appears in children after a normal birth and development. Herz included in the early type some cases starting at birth or appearing later in life in children who had abnormal neurological symptoms since birth.

ETIOLOGY

So far, no definite etiological factors have been found and the process is considered a progressive degenerative disease of the central nervous system. While the hereditary factors may be important as suggested by its frequent occurrence in people of Jewish extraction, a definite hereditary pattern has not been established.[9,10] However, occasionally it has been described in several members of a single family.

PATHOLOGY

Although no typical lesions have been found in the pathologic studies, the most frequent findings are degenerative lesions in the area of the basal ganglia with preference in the nucleus caudatus, the putamen, and the pallidus but extending, in most cases, to the lateral nucleus of the thalamus, anterior limb of the internal capsula

and even to the nucleus ruber, the subthalamic nucleus and the dentate nucleus in the cerebellum.[8,14] In some reports, changes were found extending from cortical areas to the anterior horn cells.[15] Benda,[16] in a pathological study of two cases of Dystonia Musculorum Deformans, stated that there was evidence of chronic rheumatic encephalitis. In some cases, there have been few or no pathologic changes in the brain.

The present report is concerned with thirty consecutive cases of Dystonia Musculorum Deformans, referred to the Neurosurgical Service of St. Barnabas Hospital, from February 1956 to July 1959. All the patients came to us with a confirmed diagnosis since the disease had started several years previously. Each patient was fully studied in regards to his medical and familial history along with a complete medical examination that emphasized the neurological and musculoskeletal systems. It is our purpose to present a summary of the most important findings culled from the collected material.

RACE

Of the thirty cases, only six had no definite Hebrew ancestry, the rest were of Jewish extraction. The ethnic origin of the majority were Russia, Poland, and other mid-European countries.

FAMILIAL HISTORY

In two of our patients the mother had dystonic symptoms, both mild and long standing; one of them also had a maternal cousin and a maternal uncle affected. As regards other neurological disorders; one mother had chorea as a child, in another the paternal grandparents were deaf mutes and a younger brother was a deaf mute and mongoloid. On the paternal side, one father had idiopathic epilepsy and another had siblings with convulsive and mental disorders. All the siblings of our patients and their descendents demonstrated no dystonic involvement and two of our female patients had children who appeared normal.

BIRTH AND DEVELOPMENT

There was 17 males and 13 females in the group. Pregnancy, delivery and development were in all cases within normal limits, except for a single case born prematurely at 7 months of gestation whose development, however, had been normal up to the onset of dystonia. There was no evidence of abnormal neurological symp-

toms in these patients prior to the appearance of dystonia. Mental status had been normal in all cases, prior to the onset and during the development of the illness and, in most cases, psychological testing yielded superior I.Q. ratings. Emotional problems appeared frequently and this, together with the changing pattern of the symptoms, accounted for the frequent diagnosis of hysteria in the early course of the disease.

ONSET OF D.M.D.

The age of onset of the disease, in these thirty cases, ranged between 3 and 15 years of age, with two thirds starting under the age of ten. The onset was usually unrelated to any other pathological process although, at times, it has coincided with head injuries or childhood illnesses. These processes are too frequent at this age to establish a definite etiologic relationship. However, it is possible that such events may be precipitating or aggrevating factors.

FIRST SYMPTOM

The first symptom was the appearance of involuntary motion in one part of the body. In at least 80% of the cases the foot was affected first,[17] with typical flexion inversion movements of the ankle (Figure 1). The rest of the cases started with flexion extension movements of the wrist. Only very rarely did symptoms first appear in the trunk and neck. Gradually, the involuntary motion spread to the rest of the body. The disease was progressive in all cases, although, as will be described below, the manner of involvement and the speed of progression may be different in various groups of patients.

PHYSICAL EXAMINATION

In spite of the severe involuntary movements, relatively good health is maintained, except in the most advanced cases where overexertion and difficulty in nursing care cause the patient to be severely undernourished and dehydrated.

NEUROLOGICAL EXAMINATION

The patients were found to be alert and cooperative with no impairment of hearing or vision. The speech showed, in the moderately advanced cases, a characteristic choppy articulation with occasional freezing, resembling stuttering at times. Motor power appeared normal but the performance of voluntary motion on command was

impaired by the interference of involuntary movements. Deep tendon reflexes were present and normal but, at times, were impossible to obtain or would change at different examinations mainly because the degree of initial relaxation of the extremities were different. Superficial reflexes were normal and easily obtained. No pathological reflexes were present although at times a plantar response that resembles the Babinski sign was present. However, in those cases the dystonic motion caused intermittent extension of the big toe, thus producing a Babinski-like response. Sensory examination was completely normal. Tests that involved fine coordination of motion were difficult to perform and evaluate. Balance was usually impaired by the presence of involuntary movements but, at times, even with a severly distorted posture, the patients could stand and ambulate with remarkable stability.

The positive findings in the neurological examination were limited to involuntary movements, abnormal postures, and the abnormal performance of voluntary movements on command. This latter is essentially the initial and typical symptom of the illness and we can follow the progression through the detailed study of the involuntary dystonic motion.

DYSTONIC MOTION

Dystonic motion implies an alteration of the normal distribution of tonus or resting activity of the musculature causing certain muscles to contract involuntarily. If that contraction is intermittent the result is an involuntary movement; if the contraction is maintained, with little changes in intensity, the result is a dystonic posture. These two components of dystonic activity were described by Wechsler and Brook[18] in 1912 as myostatic and myokinetic dystonia. In the present report these are referred to as "fixed" and "dynamic" dystonia. It is characteristic of dystonic motion that it disappears during sleep as do other involuntary movement disorders. A distonic motion, isolated, is difficult to differentiate from athetoid motion because in both cases there is an involuntary contraction of the muscles involved. In both, the agonist and antagonist groups of muscles are seen contracted at the same time, and there is a very similar delay in initiation and relaxation of voluntary movements which has been verified by electromyographic studies. Dystonia is characterized by the more prevalent involvement of proximal and midline parts of the body and by the typical onset and progression.

On reviewing the history of the patients, seen at different stages of the disease, the course of the illness can be reconstructed from the time of onset. The symptoms can be followed as they progress in the initially affected part and as they invade the rest of the body. Most frequently the foot is affected first. The progression of the dystonia in the foot is most demonstrative of what eventually happens in every affected area.

STAGES OF PROGRESSION

Rather arbitrarily, the progression may be divided into five stages. The change from one stage to the next is, of course, not a sudden but rather a continuous progression.

STAGE I: Dystonic, sporadic motion appears under postural stress. The patient may not show any symptom in supine, sitting or even standing positions, but while walking, the foot may occasionally, show an involuntary change of the normal posture and appear plantar flexed and inverted.

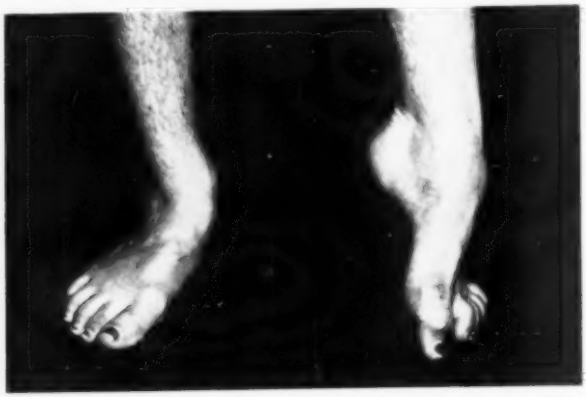


Figure 1: Fixed dystonic flexion and inversion of the ankle.

STAGE II: Dystonic posture is steadily maintained when postural stress is present. The dystonic posture is sporadic when postural stress is eliminated, although it may appear at rest under emotional stress. The patient will walk with an inverted foot but will have it completely relaxed when sitting or supine and may, occasionally when supine, show the involuntary positioning, mostly under emotional tension.

STAGE III: Dystonic posture is maintained at rest; it is difficult to

correct voluntarily or even passively. Any attempt to correct the dystonic posture will exacerbate involuntary movements during which the foot, for example, will helplessly alternate between the commanded position and the dystonic posture. "Reverse motion," described by Hunt,[19] will appear at this time. Thus, when the patient is commanded to correct the dystonic posture it becomes more severe and if asked to maintain it relaxation appears.

STAGE IV: Dystonic posture is maintained at rest and cannot be completely corrected voluntarily. Involuntary motion increases when the corrective attempt is made. The dystonic posture can not be corrected completely, passively. Pain appears at this stage and voluntary use of the limb is severely affected, in spite of the presence of normal muscular power.

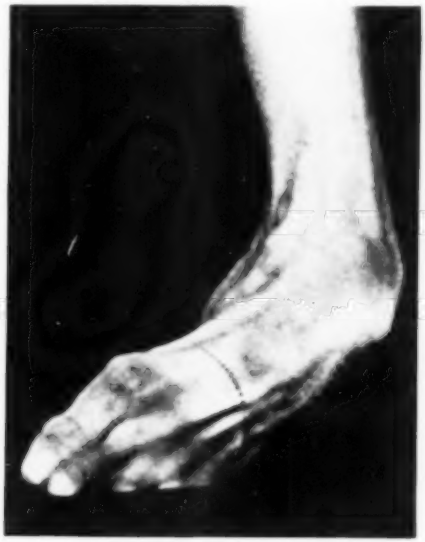


Figure 2: Fixed dystonic deformity of the foot. Semilunar foot.

STAGE V: There is decreasing dynamic dystonia and more fixed dystonic postures with increasing deformities. The deformed areas evidence apparent atrophy and loss of voluntary motion (Figure 2). This constitutes the most severe stage for any affected part. In some cases, the progress will rest in some intermediate stage for a long time, in others it will rapidly reach the most severe phase, and in any given time, several areas may be at different stages of progression.

PROGRESSION OF INVOLVEMENT

We have been dealing with the affection of single areas or parts. We will describe next the progression of involvement in the body as a whole.

1. Usually, dystonic motion appears first around a single distal joint and progresses proximally. We have found no prior predilection for the right or left side of the body.

2. The extremities that appear unaffected are usualy rather hypotonic. Some patients have even commented about the extreme flexibility of their joints prior to the onset of the illness. The extremities that appear unaffected usually show motor unrest.

3. The usual pattern is for the lower extremities to be affected first and then the upper extremities, by which time the trunk, in the lower dorsal and lumbar areas is affected.

4. The speed of progression is faster in the lower extremities than in the uppers. Thus, while the arm on the initial side is affected before the contralateral leg, there is much faster progression in the latter.

5. When the involvement is bilateral, activity is mostly centered in the proximal areas and midline of the body.

6. When the bilateral involvement has progressed to an advanced stage, other areas are involved: tongue motion, swallowing, speech, respiratory rhythm and even sphincter control.

Thus far, we have reviewed the stages and progression of severity and the manner of involvement. It appears that these can be coordinated with the pattern of involuntary motion observed. At first glance it appears that these movements are quite irregular but after observing patients at different stages of the disease one can see that there is a very definite sequence.

PATTERN OF DYSTONIC MOTION

In the lower extremities, in Stages I, II, and III, there is mostly dynamic dystonia in an alternating flexion-extension type of motion, but in Stages IV and V, hyperextension appears, leading to contractures. The foot is in plantar flexion, inversion and flexion of the knee and hip follow, causing severe lumbar lordosis (Figure 3). The hip may be fixed in slight flexion and, occasionally, dislocations occur. The knee does not remain in flexion but later on will appear hyperextended and often becomes fixed in this position. In the early stages, dystonic postures of the hip may appear in abduction or

adduction along with internal or external rotation, giving the impression of a rotary posture of the lower extremity. In most cases those dystonic postures of the hip disappear in advanced stages, unless they become fixed by contracture or dislocation of the hip joint. Thus, the most typical final fixed position of the lower extremity will produce plantar flexion and inversion of the ankle, extension of the knee and mild hip flexion, accompanied by lumbar lor-

Figure 3: Fixed dystonic flexion of the hip and knee.
Figure 4: Fixed dystonic extension of the knee.

dosis (Figure 4). In the upper extremity, involuntary flexion and extension of the wrist is likely to be the first symptom, followed by elbow flexion-extension and pronation of the forearm. The shoulder is generally internally rotated and adducted. The pattern remains dynamic during Stages I, II and III, after which fixed dystonic positions appear. The fingers then become flexed at the metacarpophalangeal joints, flexed or hyperextended at the interphalangeal joints, the thumb adducted and flexed. Flexion at the wrist, extension of the elbow, and overpronation of the forearm gives the

impression of complete rotary deformity of the arm (Figure 5). This rotary deformity of the arm is typical and may appear in some cases in a reverse pattern with external rotation of the shoulder and oversupination of the forearm. In the most advanced cases the arm may become flexed at the elbow.

Figure 5: Dynamic dystonic rotary motion of the arm. (movie frame)

In the midline of the body the earliest symptom is marked lordosis followed by hyperextension of the trunk, and the neck, during Stages I, II, and III. After Stage IV, side bending, rotation of the trunk and lateral deviations of the neck[20] appear and become progressively fixed causing severe scoliotic deformities (Figures 6). Occasionally, the trunk symptoms may be the earliest and the most rapidly progressing. In advanced cases, grimacing in the lower part of the face and frequent blinking appears, the movements of the tongue lack smooth coordination, and the speech is choppy and explosive. Incontinence and urinary retention have been observed in some far advanced cases.

The progression from the earliest symptom to the most severe form develops in some patients in 4 to 8 years. On the other hand one patient had the disease for 30 years and was not as severely involved. These and other factors demonstrate that although the symptoms and the progression followed a very similar pattern in all patients, there were some characteristics that permitted differentiation into three groups. We have classified these as childhood, adolescent and adult forms of the disease.

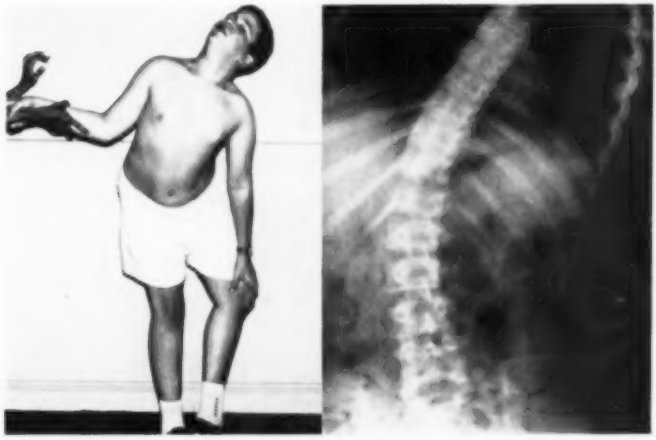


Figure 6: A—Fixed dystonic scoliosis and torticollis.
B—The x-ray film of the spine (Figure 6-A) was taken in supine position and under general anesthesia.

CLASSIFICATION

CHILDHOOD FORM: (EIGHT CASES)

This represents the most typical form of the disease and it affects the youngest group of patients. They appear normally developed for their age although they occasionally look younger. In the advanced stages they are severely undernourished (Figure 7). The onset in this group appeared from 4 to 6 years of age (with one case starting at 2½), and the initial symptom was always flexion inversion of the foot. The progression of the illness was very rapid. In our patients when first seen by us, the duration was from 2 to 8 years. In all 8 cases, the involvement was severe and bilateral, 4 to 6 years after the onset.

In this group the dynamic dystonia was maximal with minimal fixed dystonic postures. The most frequent deformity is equinovarus. Scoliosis appears in the most advanced stages. The severity

of the dystonic motion is such that in this group fractures and dislocations result quite often. These patients react with severe involuntary motion to any sensory, emotional or postural stimulus. This group reached complete functional incapacitation rapidly. Walking is rapidly impeded, there is a progressive difficulty with self-care activities and, finally, they become severe nursing problems.

ADOLESCENT FORM: (TWELVE CASES)

These patients in contrast with the childhood type, appear in a good state of nutrition, with exaggerated prepubertal characteristics. They are usually in their early teens. Most males show definite feminine-like secondary characteristics (Figure 8). The onset of the disease was from 8 to 13 years of age. The initial symptom was most frequently located in the foot but three cases started with flexion extension movements at the wrist and in one case the initial symptom was involuntary motion of the trunk and the neck. The duration of the illness, when the patients were seen, ranged from 1 to 15 years. The mean duration was 4 years.

In this group, dynamic dystonia is present only under stress and the presence of fixed dystonic postures predominate. Fixed deformities are frequent, mostly equinovarus and flexion of the hips with lordosis; scoliosis appear later. The degree of the fixed deformity is less than one would expect from the distorted posture of the patient. Hypotonia in the less effected extremities is easy to elicit in this group. The type of stimulus that will increase the dystonia in this group is emotional and postural stress. Functionally, ambulation was affected early but the upper extremities were preserved better and most patients could perform all self-care activities.

ADULT FORM: (EIGHT CASES)

The patients in this group were the oldest in the series. Their ages, when seen, ranged from 17 to 38 years. The age of onset of the disease ranged from 5 to 15 years of age and the duration from 5 to 32 years, with a mean of 15 years. The initial symptom was most frequently located at the wrist, and the feet became involved shortly afterwards. The progression is very slow and the severity of the symptoms has a migrating pattern, with long periods in which the symptoms remain static. The extremities remain mildly affected and rarely pass Stage II, while in the trunk and neck more severe dystonia and progressive deformities develop (Figure 9). Dynamic

Figure 7: Childhood form.

Figure 8: Adolescent form. Figure 9: Adult form.

dystonia is minimal, and when present it is not rare to find that the abnormal motion has a tremor-like rhythm with a slower rate than Parkinsonian tremor.

Severe fixed scoliosis and torticollis are frequently seen in this group. The type of stimulus that is most likely to bring out dystonic symptoms in these patients is postural stress. Pain was never present as a main complaint. Functionally, these patients remain remarkably independent, they can usually ambulate with a very

abnormal gait ("dromedary gait") but still maintain good balance. The voluntary use of their limbs is not affected as in the other groups, and in spite of the abnormal movements all of these patients were independent in self-care.

Although most of the patients were fitted into one of the three groups described above, there were obviously cases that demonstrated some overlapping. However, the differentiation of the form of the disease in any individual case will help in establishing a long range prognosis and aid the therapeutic management of the patient.

DRUG THERAPY

There is no drug at the present time that can stop or reverse the symptoms of Dystonia Musculorum Deformans. However, good therapeutic management can make patients' lives more comfortable. Drugs of the anti-parkinsonian type have been recommended in the past. They have very little, if any, effect, on these cases. The use of drugs of the chlorpromazine group may be helpful, particularly in patients in whom emotional stimulus increases the dystonic symptoms. In advanced cases, only drugs that can cause drowsiness (even to the point of sleep) can placate the severe involuntary motion. Thus, tranquilizers, in large doses, can be as effective as an equivalent dose of barbiturates. The present muscle-relaxant drugs have no effect.

REHABILITATION

Physical therapy and other rehabilitation techniques can help in the overall management. The main principle to keep in mind is that only relaxation-inducing therapy can accomplish any practical improvement in these patients. This can only be done in the early stages and mostly in the adolescent and adult groups. When the abnormal movements are very active, as in the childhood group or in very advanced stages, any stimulus that will act as a sensory stimulation will increase the severity of the symptoms. When it is possible to find the posture of maximum relaxation or to induce it by means such as hydrotherapy, the therapist will be able to take the joints through the range of motion and prevent the development of fixed deformities. In many instances, when attempts were made to correct the fixed deformities by means of braces or static devices, the results were not satisfactory and the patient either could not tolerate the brace at all because it caused pain and discomfort, or the patient complained of further impairment of gen-

eral functioning. It should be emphasized that except for attempting to prevent the development of fixed deformities, there is little else that can be accomplished pre-operatively by physical therapy. In the post-operative phase, rehabilitation may be extremely helpful.

CORRECTIVE SURGERY

Any surgical intervention directed towards the prevention or correction of deformities is contraindicated if there is evidence of dystonic activity in the part to be operated upon. It is obvious that correcting the position of the joint or bone does not eliminate the abnormal activity of the muscles surrounding it. Moreover, it appears that if abnormal activity is restrained at the joint, the involuntary motion becomes more severe in the surrounding areas. For example, we have seen a case in which fixation of the wrist in a functional position was carried out to eliminate involuntary motion at this point. However, the patient could no longer use the arm because severe dystonic postures and later contractures developed in the fingers, elbow and shoulder. In some cases in which braces were used to immobilize the joint, they had to be removed because of the exacerbation of the symptoms. However, when the joint is immobilized surgically the situation can not be reversed.

When section or lengthening of tendons has been carried out to correct dystonic activity, the deformities reappeared after surgery.

Neurectomies and root sections are generally of no practical value because they attack the problem of a generalized disease in a very limited area.

NEUROSURGERY

Different types of operations upon the central nervous system have been employed.[21,22] Some of them attack the pyramidal tract either at its origin in the cortex, in the midbrain or in the spinal cord. These appear to be effective in relieving hyperkineses in direct proportion to the degree of motor weakness produced. Therefore, these procedures are of limited practical value as far as improving the function of the patient.

It has been demonstrated that lesions can be placed in the area of the basal ganglia and relieve the involuntary motion without producing any neurological deficit.

The investigation carried out at this center demonstrates that

Dystonia Musculorum Deformans can be alleviated by lesions placed in the globus pallidus and/or ventrolateral area of the thalamus. Chemopallidectomy is a neurosurgical procedure involving the injection of small amounts of absolute alcohol, or a special alcohol solution, into the globulus pallidus. The surgical technique of chemopallidectomy and chemothalamectomy, together with documented case reports, have been discussed in previous reports from this center.[23,24]

Most of the patients included in this clinical study underwent chemopallidectomy and/or chemothalamectomy. The results have been very encouraging and have permitted some of these children to return to normal life after years of incapacitation and suffering. Some of these children underwent chemopallidectomy and/or chemothalamectomy three years ago and our follow-up studies indicate that the relief of the symptoms of Dystonia Musculorum Deformans has persisted up to the present time.

SUMMARY

A clinical study of thirty cases of Dystonia Musculorum Deformans was presented. Although the pattern of abnormal movements and deformities was quite similar in all cases, remarkable differences in the clinical course make possible the classification of Dystonia Musculorum Deformans into three groups: childhood, adolescent and adult forms of the disease. Therapeutic measures found most useful in the management of these cases are described. The treatment of choice for Dystonia Musculorum Deformans is chemopallidectomy and/or chemothalamectomy.

REFERENCES

1. Schwalbe M. W.: Eine eigentumliche tonische Krampform mit hysterischen Symptomen, Inaug. Dissert., Berline, G. Schade, 1908.
2. Ziemen, T.: Fall von tonischer Torsionneurose, Neurol. Centralbl. 3:109, 1911.
3. Oppenheim, H.: Ueber eine eigenartige Krampfkrankheit des Kindlichen und jugendlichen Alters (Dysbasia lordotica progressiva, dystonia musculorum deformans), Neurol. Centralbl. 30:309, 1911.
4. Fraenkel, J.: Dysbasia lordotica progressiva, dystonia musculorum deformans, torticpalyes, Jour. Nerv. and Ment. Dis. 1912, XXXIX, 361.
5. Kaufman, M. R.; Savitsky, N. and Fried, J. R.: Dystonia musculorum deformans of encephalitic etiology, Arch. Neurol. and Psyiliat. 20:824, 1928.
6. Lwoff, Cornill and Tarbowla R.: Spasme de torsion d'origine infectieure Rev. Neurol. 1922, XXXVIII, 1429.
7. Alexander, L.: The fundamental types of histopathological changes encountered in cases of athetosis and paralysis agitans. A. Research Nerv. and Ment. Dis. Proc. (1940) 21:334, 1942.
8. Herz, E.: Dystonia. Arch. Neurol. and Psychiat. 1944, LI, 305 and 319; LII, 20.
9. Meyers, R.: Clinical Neurology, edited by A. B. Baker. Vol. 2 pp 1107-1159, 1955 (Harper).
10. Diseases of basal ganglia and subthalamic nuclei. The Oxford Medicine. Volume VI, 1949. Chapter XI, 261.

11. Carpenter, M. D.: Athetosis and the basal ganglia. Review of literature and study of forty-two cases. Arch. Neurol. and Psychiat. 1922, VIII, 538.

12. Dimitri, V.: Un caso de distonia muscular deformante, estudio anatomoclinico. Semana medica 1932, I, 428. Segunda observacion anatomoclinica de distonia muscular deformante. Semana medica 1935, I, 77.

13. Nielsen, J. M.: Autopsy in a case of dystonia musculorum deformans. Bull. Los Angeles Neurol. Soc. 1941, VI, 87.

14. Davison, C. and Goodhart, S. P.: Dystonia Musculorum Deformans Arch. Neurol. and Psychiat. Jan.-June 1933: 1109.

15. Davison, C. and Goodhart, S. P.: Dystonia Musculorum Deformans: Clinicopathologic Study. Arch. Neurol. and Phychiat. 39:939 (May) 1938.

16. Benda E. Clemens: Chronic Rheumatic encephalitis. Arch. Neurol. and Psychiat. 4:417, 1920.

17. Goodharts P. and Frans W. M.: On the deformity of the foot in Dystonia Musculorum Deformans. Arch. Neurol. and Psychiat. 1924, XI, 436.

18. Wechler and Brock: Dystonia Musculorum Deformans. Arch. Neurol. and Psychiat. 1922, VIII, 538.

19. Hunt, J. R.: The progressive torsion spasm of childhood. Journal Am. Med. Assoc. 1916, LXVII, 1450.

20. Herz and Hoefer: Spasmodic torticollis: I Physiologic analysis of involuntary motor activity. Arch. Neurol. and Psychiat. 61:429; 1949.

21. Tracy J. Putnam: Treatment of athetosis and dystonia by section of extrapyramidal tracts. Arch. Neurol. and Psychiat. 1933, 505.

22. Klemme, R. M.: Surgical treatment of dystonia with report of one hundred cases. Res. Publ. Assoc. Nerv. and Ment. Dis. 1942, XXI, 596.

23. Cooper, I. S.: Relief of Juvenile Involuntary Disorders by Chemopallidectomy. J.A.M.A. July 20, 1957, Vol. 164.

24. Cooper, I. S.: Dystonia Musculorum Deformans Alleviated by Chemopallidectomy and Chemothalamectomy. A.M.A. Arch. Neurol. and Psychiat. Vol. 81 pp. 5-19; 1959.

Note: A 16 mm. sound movie entitled "Dystonia Musculorum Deformans: Progression and Forms of the Disease" will be available upon request from the Photographic Library of the Neurosurgical Service of St. Barnabas Hospital.

400 East 34th Street, New York 16

Otological Findings in Birth Injuries of the Newborn*

Part II . . . Continuation of a Study, with Discussion and Review of the Literature (Part I devoted to Experimental and Clinical Observations, appeared in the December 1959 issue.)

J. Berberich, M.D.†
New York

The mortality rate of newborn and young infants, and especially of the premature, is still high, as compared to total mortality rates. Ylppö ascribed the high mortality rate in the premature to cerebral birth injury which produced pial and ventricular hemorrhages. In his large series, the mortality rate during the first year of life of infants with a birth weight of 600 to 1,000 Gm. was 94.4 per cent, and of those with a birth weight of 2,000 to 2,500 Gm. 33.5 per cent; the mortality rate of the two groups of these premature infants was 53.5 per cent. Schwartz's studies further established the presence of focal cerebral hemorrhages and areas of softening in 65 per cent of premature and full-term infants. His theory, now amply proved experimentally, is that the hemorrhages and focal necrosis and softening are caused by the effect of the difference between the atmospheric pressure on the presenting part (the head in 95 to 97 per cent of births) in the external uterine orifice and the intrauterine pressure on the rest of the fetus. In this type of birth injury, the duration and difficulty of labor and pelvic size play important roles. So long as the amniotic sac is intact, the fetus is under a uniform intrauterine pressure ranging from 80 to 250 mm. When the sac bursts and the presenting part emerges, thereby closing the uterine orifice like a ball valve, the head is suddenly exposed to the lower atmospheric pressure. The effect can be likened to that of a suction cup applied to the skin, and has been proved experimentally in animals and infants. Caput succedaneum and cephalhematoma are two of the conditions resulting from exposure of the head to atmospheric pressure during birth.

* This paper is based on our own experimental and clinical investigations and is supplemented by the more recent literature.

† Professor for ENT, University of Frankfurt am Main; Research Associate for ENT, Mt. Sinai Hospital, New York.

Since the dural veins, the superior longitudinal sinus, and the large and small fontanels are directly connected to the scalp veins they are influenced by changes in these veins but, they are also directly affected by the difference in pressures, so that overfilling, congestion, stasis, stretching, and tearing of dural, pial, and cerebral blood vessels, and often thromboses, occur. Schwartz divides birth injury lesions into those due to mechanical factors and those which develop elsewhere than at the site of injury, for example, disturbances or damage of cerebral regulatory centers. In these cases, such conditions as metabolic disorders, sugar control or abnormal sexual development may be the secondary consequences of birth injury.

The repeated stressing of the importance of birth injury by Ylppö, Dollinger, and Schwartz and co-workers, who based their concepts on their clinical, pathologicanatomic, and experimental investigations, have made an important contribution to the explanation of many pediatric and neurologic conditions.

Spurred by these concepts of the mechanism of birth injury, we undertook an experimental and clinical study of the problem as it related to its otologic effects. The clinical investigation, comprising a series of 190 cases, and carried out as a cooperative effort of several departments of the Frankfurt University Hospitals, drew upon the technics used for the study of concussion, skull and brain injuries, and brain tumors.

The animal experiments with puppies, kittens, and rabbits tried to reproduce the mechanism of head injury in human birth by the application of a suction cup with manometer to the scalp in the area of the longitudinal sinus. We proved that the degree and extent of the thrombosis in the dural veins, the necrotic foci in the brain, and the hemorrhages in the inner and middle ear structures depended on the intensity and duration of the experimentally produced suction, i.e., negative pressure. Histologic examination of the petrous bones revealed hemorrhages like those which Voss found in newborn infants. In the animals whose brains were injured by the insertion of a sharp needle, foci of fat cells were found in the injured area similar to those we found in infants with cerebral birth injury.

Circulatory studies in the cadavers of children and adults, by means of a gelatin and red oxide of lead mixture which solidified within minutes after injection into the longitudinal sinus, showed that the venous system of dura, pia, brain, petrous bone (including the inner and middle ear), pituitary gland, and eye was a closed

system draining into the longitudinal sinus and from there into the jugular vein. Our theory that birth trauma of the large or small fontanels or longitudinal sinus could lead to stasis and other changes in the pituitary gland, ear, or eye was thus confirmed. A study of the pituitary glands of 40 nonsyphilitic newborn infants gave additional proof. Histologic examination showed in addition to hyperemia and hemorrhages, atrophy and even disappearance of cellular trabeculae and necrosis. These findings seemed particularly significant since they may possibly explain certain cases of dwarfism, myxedema, dystrophia adiposogenitalis, and juvenile diabetes.

Analysis of the results of the clinical study clearly revealed that the clinical picture did not necessarily mirror the severity and extent of the cerebral injury. Massive lesions were found at necropsy of children who had presented the same clinical picture as children with considerably slighter damage. Nor were the pathologic reflexes more varied or more marked in the group with severe damage than in the others.

A spontaneous horizontal nystagmus to one or both sides, present in 80 per cent of the newborn regardless of birth weight, was one of the most important signs. It was apparent immediately after birth, was marked during the first few days, and slowly diminished in intensity until its eventual disappearance. In most the nystagmus lasted for 2 to 3 months, but in a few children followed for periods up to several years the nystagmus lasted for 5 to 12 months or even longer. Spontaneous nystagmus in older children was often present in those who survived with sequellae such as spasmophilia, neuropathy, convulsive disorders, or idiocy. The assumption seems justified that spontaneous nystagmus, particularly of the vertical type, in older children may be the result of injury at birth either of the peripheral labyrinthine structures of the vestibular nuclei. Recovery from the peripheral injury may possibly be easier than from injury of the central nervous system. Experience with concussion in adults and the presence of cerebral scars in children with birth injury point to this concept.

In many cases, only a spontaneous eyeball deviation rather than nystagmus was seen, or a deviation instead of nystagmus after labryinthine stimulation, or even concurrent deviation and nystagmus. In the evaluation of our findings we considered the deviation as an equivalent of nystagmus, an opinion now almost generally accepted by otologists.

The frequent absence of response to caloric stimulation and the

weak response to rotatory stimuli, without relation to birth weight or age, were striking. These reactions, therefore, apparently do not depend on the stage of cerebral development in the newborn. Caloric nonresponse was found mainly in children with central nervous system disorders, such as spasmophilia, epilepsy, and severe mental defects. Often spontaneous nystagmus, absence of response to caloric stimulation, and rotatory hypoirritability were all present in the child. The term "birth injury syndrome" therefore occurs to us as adequately describing a condition in which spontaneous nystagmus, caloric nonresponse, rotatory hypoirritability, and various other signs of central nervous system injury are present.

The first appearance of a normal caloric reaction often occurs at the age of 3 to 4 months, in other words, after the spontaneous nystagmus has subsided.

The rotatory tests gave no such unequivocal results as the response to caloric stimulation. After rotation in all 3 positions, most children had a definite postrotatory nystagmus, although of shorter duration than normal. No response whatever could be elicited only in a few of the children classified as idiots. No doubt, rotation is the more physiologic and stronger labyrinthine stimulant, and may therefore account for the difference in the results of the two tests. Absence or weakness of rotatory reaction can also be of peripheral or central nervous system origin. The normal rotatory reaction appears 5 to 6 months after birth, therefore also after the disappearance of spontaneous nystagmus.

It is noteworthy that the appearance of normal labyrinthine function at 4 to 6 months of age, as judged by the response to experimental stimulation, is accompanied by the decrease or disappearance of general and focal symptoms. The facial pallor and masklike appearance are replaced by a normal appearance, respiration becomes more regular and deeper, feeding improves and there is weight gain, the temperature becomes normal, and only rarely are singultus, yawning, stupor or convulsions observed.

The decrease or disappearance of the clinical, neurologic and otologic manifestations in most of the children at about the same age after birth is unmistakable evidence that the cause is an injury of the central nervous system sustained during birth. If the injury produces cerebral scarring as it heals, sequellae remain throughout life.

There is an enormous literature on the anatomic and neurologic aspects of birth injury, but its otologic aspects have received com-

paratively little attention. From a bibliography which Schwartz has recently compiled, covering the literature of the past 100 years in all languages, it is apparent that birth injury is rapidly gaining increased recognition. The relation of speech defects or such neurologic disorders as Little's disease, spasmophilia, pareses, hemiplegias, and syringomyelia to birth injury is now realized. Pathologists, by demonstrating iron deposits, and old foci of softening with varying degrees of lobar destruction (porencephaly) in the brains of older children have made a signal contribution to our knowledge of birth injury. Clinical diagnoses of debility, atrophy, dyspeptic disturbances, nutritional disorders, and terminal broncho-pneumonia have fallen into disrepute. Wiechers[103] and Von Pfaundler[64,65] were the first to recognize that such terms were meaningless catch phrases and that the clinical features were actually signs and symptoms of birth injury.

Wolpert[105] has demonstrated this to be true of another manifestation in the newborn. Like Schwartz, he holds that the peculiar movements of the extremities, fingers, and toes often seen in newborn infants closely resemble those of adults with lesions of the basal ganglia after concussion or cerebral trauma, and that the cause is birth injury rather than immaturity of the central nervous system.

Awareness of birth injury of other organs—various endocrine glands, the lungs, liver, kidneys, pancreas—has increased. Schwartz and his associates found metabolic disturbances due to birth injury which seem to explain the etiology of icterus neonatorum.

Recognition of the cerebral changes caused by birth injury is greatly aided by electroencephalography. Hughes and co-workers[46,50] found various electroencephalographic abnormalities in 8 children; 7 of them also had neurologic signs of injury. They believe that this method might disclose cortical changes before neurologic changes occur, and remain after the neurologic disturbances have disappeared. Aird and Cohen[1] are of the same opinion. Gurdjian and Webster[41] state that the electroencephalographic pattern of infants with birth injuries is difficult to evaluate because the normal range in this age group is still not definitely known. On the other hand, Hill and Parr[44] believe that electroencephalography may reveal the irreversible damage caused by prenatal and birth trauma.*

* When I was reading the galleys of this paper, I found a letter from England in the Journal of the Americ. Med. Assoc. 171, No. 4, 1959 (Sept. 26, 1959) stating the good results with the use of a vacuum-extractor as a replacement of the traction forceps (T. Malmstrom, W. D. Cunningham, O.G.A. Berggren).

The problem of deaf-mutism as related to birth injury is of particular interest to otologists. The possibility was suggested by Voss many years ago. Often, so-called congenital deafness cannot be explained on the basis of intrauterine noxae, maternal infections, or heredity, since the histories reveal no such clues. Recovery from a silent or unrecognized meningitis or otitis media is often assumed in such cases. Detailed examination as early as possible, and with all available methods, of all deaf-and-dumb children might produce considerable information on the etiology, and provide the means of differentiating peripheral from central nervous system deafness. The earlier the examination, the sooner the correct diagnosis might be established. Unfortunately, the suspicion of deaf-mutism arises when the child is about 3 years old or even older and has not begun to speak. Present knowledge allows the assumption that birth injury may cause peripheral deafness by hemorrhage into the labyrinth or the acoustic nerves or central nervous system deafness by damage of the auditory pathways or the hearing center. One can draw a close analogy to speech defects resulting from birth injury.

Lable[54] found hereditary deaf-mutism in 13 per cent of a series he studied, and assumed congenital factors in 57 per cent; but he did not mention birth injury. Winnewisser[104] examined 300 deaf-mute children; in 13.5 per cent the condition was hereditary, and in 22.8 per cent postnatal exogenous factors were responsible; 40 per cent of the children were first born; many of the children were also of subnormal intelligence. In his opinion, inner ear damage due to birth injury might well play an important role in the etiology of deaf-mutism, particularly in the first born, in whom the likelihood of birth injury is greatest.

Obviously, there are no clear indications of the etiology in a high percentage of deaf-mute children. Not until the petrous bones and brains of large series of such children have been carefully examined will the question of etiology be clearly answered. How great the amount of study remains to be done in the field of pediatric and otologic practice may be judged from what still must be done in this small segment of the problem.

Review of the Literature

As early as 1907, Seitz[79,80,81,82] had noted the wide variety of intracranial lesions in the newborn, and their relation to trauma of the larger blood vessels and brain. The occurrence of pial and cerebral hemorrhages, he emphasized, depended both on the length of labor and the relation between the presenting head and the cervix. Asphyxia, he belived was the most important sign of the clinical picture of birth injury; the next important

was an increase in blood pressure resulting from irritation of the vasomotor center, which could easily lead to further bleeding. Pronounced restlessness, facial grimaces, frequent crying, poor feeding, rare vomiting, pallor, and the absence of the sucking or buccal reflex he listed as characteristic signs. Later, general and focal symptoms of intracranial pressure appeared. The general symptoms were increased blood pressure, slowed pulse rate, hyperreflexia, increased irritability and sensory state, disturbed respiration (deep, slow, and sometimes interrupted), unconsciousness, myriasis, trismus, facial paralysis, hemiplegia, paraplegia, strabismus, and miosis. In those who did not die soon after birth, the irritative state passed gradually into a paralytic one, the convulsions became less frequent, the cyanosis more pronounced, the pupils more dilated and without reaction, the respiration assumed a Cheyne-Stokes character and finally ceased.

In 1919, Ylppö[100,102,103] concluded that the diagnosis of debility and lack of capacity for extrauterine life was an unproved concept. He believed that in most cases of neonatal death the cause was birth injury. Furthermore, in such children who survived the later appearance of central nervous system disorders, primarily Little's disease and mental defects in the absence of other cerebral manifestations, were most likely due to cerebral injury during birth. He found that of 300 premature infants followed for several years, 7.4 per cent were idiots or imbeciles.

Dollinger[57] investigated the relation of imbecility to possible birth injury in a large series of older children. In all of them the imbecility was congenital or had appeared early in life. Of 78 imbeciles, 28 (40 per cent) had been premature infants. He stated: "Most factors believed to be responsible for imbecility must be regarded as unproved; they are all concepts built up as a result of traditional ways of thinking, supported neither by pathologic findings nor clinical experience." His views on the clinical picture of birth injury agree with those of Seitz and Ylppö.

Benda[5] in a report on 100 cases of mental deficiency that came to autopsy stated that birth injury was held to be the cause of 30 to 35 per cent of the idiot group, in 8 per cent of the imbecile group, and an even lower percentage of the moron group.

Only a few of the German textbooks of that period even mentioned birth injury (von Reuss,[98] Finklestein,[32] Meyer[80]).

The otologic aspects of birth injury at first received scant attention. Knvirt[69] suggested that the hearing of a normal newborn is no different from that of an adult, although it might not be as acute in the first few hours after birth. Demetriades[20] established the absence of the auropalpebral reflex in the first postnatal hours, and even much longer, particularly in the premature. He suggested that birth injury might explain such absence.

Until Voss[108] demonstrated the relation of vestibular disturbances to birth injury, there were practically no reports on this aspect of birth injury, although a few investigators (Alexander[1], Bartels[2,3], Schur[94]) had tried to establish normal levels of caloric and rotatory excitability in the newborn. Alexander used the rotating chair test and found that 78 per cent of 132 newborn infants reacted "normally" and 22 per cent "abnormally" with regard to nystagmus and head movement. In his opinion, absence of nystagmus was the most important "abnormal" reaction; apparently, he was unaware of the frequent presence of spontaneous nystagmus. Schur examined 20 older children, and, unlike Alexander, most of them in upright position with the head not fixed, so that his results differed from Alexander's. When he examined the children in the recumbent position, with head fixed (as Alexander had done), he got the same results as Alexander. Of the 20 children, 75 percent showed Alexander's "abnormal" reaction, i.e., absence of postratatory nystagmus but head turning and eyeball deviation during rotation. We believe, unlike Alexander and Schur, that eyeball deviation should be interpreted as the equivalent of nystagmus. The spontaneous nystagmus of the newborn Schur ascribed to nuclear disturbances affecting of ocular muscles.

Thornval (1921[99]) obtained a response to caloric stimulation in 74 newborn infants; he suggested that the reaction was the same as of adults under

general anesthesia. Kleitman and deKleyn[39] attempted to clarify the role of asphyxia in vestibular nystagmus, and finally concluded that the site of injury must be in the medulla oblongata. Cords[40-42] reported that in adults with head injury the nystagmus was due to damage of the peripheral labyrinth or to frontal lobe trauma. This is now generally known to be true, and has been found in head injury, brain tumors, and intracranial mass lesions. Galebsky[43] reported normal vestibular reactions in 100 children, whereas Froding[29] in a series of 31 children with cerebral birth injury found 4 with severely impaired reactions to caloric and rotatory stimulation and 6 with milder impairment. Ehrenfest[30] found spontaneous nystagmus in 35 per cent of infants born normally, but in 100 per cent in those with abnormal presentation in birth.

Pinhard (1928[44]) reexamined the infants we had studied in 1922-1923, by which time they had reached the age of 3½ to 6 years. In the interval, 22 of the original series of 75 children had died and 27 were not available for reexamination. Of the 26 children, 15 had been premature.

Summary of his results: Most of these re-examined children was first born, very few were the second, third, fifth or six child. ¼ of these follow-up children still showed spontaneous nystagmus; 50% of the children revealed a pathological reaction to the caloric or rotatory stimulation or to both in the sense of a reduced or even completely missing labrinthine response.

6 of the 26 children showed an outspoken mental retardation, 2 of them with marked speech defects. In a very few cases Pinhard found convulsions, pointed head, impaired hearing, facial or abducens paresis.

Ross[31] studied a series of 23 children between 2 and 12 years of age, of whom 20 had been premature. The response to vestibular stimulation was normal in 11, although spontaneous nystagmus and past-pointing was found in some; 3 of the 11 were mentally retarded. The other 12 children had an abnormal reaction; 5 had spontaneous nystagmus, and 3 were mentally retarded.

Preechtel[45] found changes in the inner ear in 4 of 5 infants with severe motor disturbances (static disturbances, inability to sit up, stand, or walk, and some speech anomalies).

Albrecht[2], after examining the petrous bones of 80 infants and children, confirmed the finding of Voss and his school that hemorrhages in the ear due to birth injury are frequently present. He stressed the importance of severe hemorrhages in the internal meatus; in 31 of his cases, the hemorrhage had damaged the acoustic nerve. He suggested that bleeding due to birth injury into the tissue cushion in the middle ear might later cause fibrosis of the middle ear mucous membrane, and play a role in otitis media in infants. Fragility of the blood vessels, in his opinion, might be a factor in aural hemorrhage in the newborn.

An interesting contribution to the problem of ear involvement in birth injury was made by Barth[3]. Histologic study of the petrous bones of 26 newborn infants confirmed our findings, but he believed that asphyxia played the important role rather than birth injury as such. He based his theory on the results of an experiment in which he killed 3 pregnant guinea pigs with carbon dioxide; none of the 7 fetuses showed birth injury or cerebral hemorrhage, but hemorrhages in the ear were present. We, too, found that asphyxia can occasionally cause hemorrhages in various organs, including the ear, but firmly believe that the asphyxia, like the hemorrhages in brain and ear, can be the result of birth injury. In any event, Thieleman[32] confirmed our experimental and Albrecht[2] our anatomic findings. Barth simply accepts the presence of asphyxia without trying to explain its cause.

Catel[5-22] had found spontaneous nystagmus in 66 per cent of premature infants whose birth had been clinically normal, Barth[3] in 74 per cent of infants, and we in 80 per cent. The observations on the appearance and course of the spontaneous nystagmus by Catel[21-22], Barth[3], and Henkel[11] agree with ours, but they believed that it was a physiologic phenomenon, while we think it is a pathologic one. Catel compared the spontaneous nystagmus of infants with

that of miners with an additional "increased irritability of the vestibular apparatus." Bartels did not accept this explanation, and instead compared infantile spontaneous nystagmus to that of the blind; in both types he thought the cause to be an irritability of subcortical centers.

A long-term study by Naujoks[42] of infants with signs of intracranial hemorrhage after birth is noteworthy. While some of them died of the damage during the following weeks, months or years, most of them survived and when examined after many years were found to be healthy.

Catel[22], on the basis of the ration of serum bilirubin to cerebrospinal fluid bilirubin, held that the presence or absence of intracranial hemorrhage during birth could be established. A return of the ratio to normal after birth he believed was proof that intracranial bleeding had stopped.

The disadvantage of all of the reports cited is that the series investigated are too small to provide a definitive answer. Schwartz's data, on the other hand, comprising an enormous series gathered in the course of 35 years, cannot be ignored, nor his findings explained on the basis of asphyxia alone.

Kelemen[31] found aural hemorrhages in newborn infants with skull fracture or skull perforation. Crothers[25] holds that the differences in pressure to which the fetus is subjected during birth is an important cause of intracerebral and intraventricular bleeding. Lawrence and Feind[35] have found no postrotational nystagmus in the newborn, but do not mention eyeball deviation.

Ford[20,32,38] pointed out that while hemorrhages are found in a large percentage of infants at birth or during the first 2 weeks, they are severe enough to be considered the cause of death only in 33 per cent.

In addition Ford[32] found that of 200 infants with bilateral spastic paralysis, 33 per cent were premature and in 15 per cent delivery had been difficult.

Förster's investigation of striate motor disturbances are pertinent here, since the athetotic movements, variations in muscle tone, and paraplegias in newborn infants can be traced to lesions in the globus pallidus. According to Förster, Little's disease is often found in premature infants, and forceps delivery may be one of the causes.

Gurdjian and Webster[41] believe that the following pathologic abnormalities may be found in infants surviving intracranial injury at birth: cortical lesions eventually leading to atrophy or cyst formation, ventricular distortions, subdural hematomas; calcified hematomas, thickening of the arachnoid, external hydrocephalus, and porencephalaic cysts.

Fisher's[28] summary of the pathologic reactions elicited in clinical and experimental tests of vestibular function may be useful:

1. Absence of nystagmus after stimulation of the labyrinth speaks for a central lesion somewhere between the vestibular nuclei and eye nuclei.

2. Absence of caloric reaction in the presence of normal turning reaction is found in inner ear syphilis, serous labyrinthitis, trauma of the skull.

3. Absence of turning reaction in the presence of normal caloric response speaks for inner ear syphilis with pathological changes in the nerve endings of the peripheral sense organ (crista ampullaris in the semicircular canal). (Some believe that this discrepancy between loss of rotatory reaction and normal caloric response is proof that the two stimuli do not act upon the same place in the central vestibular apparatus.)

4. Loss of caloric and rotatory reaction speaks for an involvement of the retrolabyrinthine part of the vestibular apparatus.

5. Reactive dissociation is a term which is used when the one labyrinth reacts much better to turning stimuli and the other reacts better to caloric stimuli. It is supposed to be a sign of a central lesion.

6. Labyrinthine hyperexcitability is a diagnosis which experienced otologists avoid because the range of variations in the so-called normal reactions is wide. Fischer accepts it only when spontaneous nystagmus is present. True hyperirritability is mostly of central nervous system origin due to lesions in the central vestibular nuclei, the central pathways, or the central regulating mechanism. In some cases, the hyperirritability is of peripheral labyrinthine origin, as in the beginning of an infectious labyrinthitis or Menière's.

Hyperirritability of central nervous system origin occurs with lesions in the posterior fossa in cases of skull fracture, encephalitis, disseminated sclerosis, vascular disturbances, and in all cases with increased intracranial pressure.

7. Hypoexcitability is combined with deafness of the same ear, the presence of a peripheral lesion, i.e., of the labyrinth itself, is assumed. In lesions of the posterior fossa with increased pressure for a longer time hypo, irritability of central origin might also be found.

8. Conjugate deviation which occurs after cold stimulation of an ear: the eyeballs show deviation toward the stimulated ear followed by a nystagmus to the opposite side; it speaks for a central lesion in the supranuclear region, especially of the brain tem and the pons.

In summary, the few early clinicians who were at all interested in birth injury were primarily concerned with pathologic features, and simply noted the clinical manifestations without systematic investigation. Dollinger alone tried to follow his cases for possible sequellae in order to establish the relation between birth injury and imbecility or idiocy. Almost all of the later reports confirmed the results of our investigations. Some, however, believe that asphyxia rather than birth injury plays the primary role and that spontaneous nystagmus in the newborn is physiologic; but they do not explain the cause of the asphyxia.

REFERENCES

1. Aird, R. B., and Cohen, P.: Electroencephalography in cerebral palsy. J. Ped. 17:448, 1950.
2. Albrecht, W.: Die geburtstraumatischen Schadigungen des Ohres. Ztschr. Hals-, Nasen u.Ohrenh. 27:495, 1930.
3. Alexander, G.: Die Reflexerregbarkeit des Ohrlabyrinthes am menschlichen Neugeborenen. Ztschr. Psychol. u.Physiol. Sinnesorg. II Abt. 45:153, 1910-1911.
4. Bartels, M.: Uber Regulierung der Augenstellung durch den Ohrapparat. Arch. Ophthal. 76:1,1910. 77:531,1910. 78:129,1911.
5. Bartels, M.: Corticale Augenabweichung. Klin. Monatbl. Augenh. 62:673,1919.
6. Bartels, M.: Die Reflexbahnen für die Ohr-Augenbewegungen. Arch. Ophthal. 117:538,1926.
7. Barth, H.: Zur Frage Geburtstrauma und Gehörorgan. Ztschr. Hals- Nasen- u.Ohrenh. 35:1, 1933.
8. Benda, C. E.: The late effects of cerebral birth injuries. Medicine 24:71, 1945.
9. Benecke, R.: Über Tentoriumzerreissungen bei der Geburt, sowie die Bedeutung der Duraspannung für die chronische Gehirnerkrankungen. Münch. med. Woch. 57:2125, 1910.
10. Berberich, J.: Tierexperimentelle Untersuchungen über das Geburtstrauma. Verhl. südwestdeutscher Hals-Nasen-Ohrenärzte 1924.
11. Berberich, J.: Experimentelle Untersuchungen über das Geburtstrauma des Felsenbeines. D. med. Woch. 51:1726, 1925.
12. Berberich, J.: Geburtstraumatische Veränderungen der Hypophyse. Monatschr. Kinderhl. 34:595, 1925.
13. Berberich, J.: Besteht ein Zusammenhang zwischen Fettbefunden im Zentralnervensystem neugeborener Menschen und der Markscheidenentwicklung. Klin. Woch. 5:211, 1926.
14. Berberich, J. and Bär, R.: Fettbefunde im Gehirn fötaler und neugeborener Tiere. Münch. med. Woch. 31:1287, 1925.
15. Berberich, J. and Hirsch, S. R.: Die Roentgenographische Darstellung der der Arterien und Venen am lebenden Menschen. Klin. Woch. 2:2226, 1923.
16. Berberich, J. and Hirsch, S. R.: Beitrag zur Frage der multiplen Blutdrüsensklerose. Klin. Woch. 3:483, 1925.
17. Berberich, J., and Kelemen, G.: Erkrankungen des Ohres, in *Pathologie der Laboratoriumstiere* (Cohrs, P., Jaffe, R., and Meesen, H., eds.) Berlin: Springer Verlag, 1958, Vol. 1, pp. 670-698.
18. Berberich, J. and Stern, M.: Beitrag zur Mechanik der Entstehung geburtstraumatischer Felsenbeinblutungen. Ztschr. Ohrenk. 11:385, 1925.
19. Berberich, J. and Wiechers, A.: Zur Symptomatologie des Geburtstraumas. Ztschr. Kinderh. 38:59, 1924.
20. Brock, S. et al.: *Injuries of the Skull, Brain and Spinal Cord* (3rd ed.) Baltimore, Williams & Wilkins, 1949.
21. Catel, W.: Neurologische Untersuchungen an frühgeborenen Kindern. Monatsschr. Kinderh. 38:303, 1928.
22. Catel, W.: Zur klinischen Diagnose intrakranieller Geburtsblutungen. Monatsschr. Kinderh. 52:1, 1932.

23. Cords, R.: Optisch-motorisches Feld und optisch-motorische Bahn. Arch. Ophth. 117:38, 1926.

24. Cords, R.: Zur Pathologie der Führungsbewegungen. Arch. Ophth. 123:173, 1929.

25. Crothers, B.: Changes in pressure inside the foetal cranio-vertebral cavity. Surg., Gynec., & Obst. 37:790, 1923.

26. Demetriades, T.: Der cochleopalpebrale Reflex bei Neugeborenen. Monatsschr. Ohrenh. 55:756, 1921.

27. Dollinger, A.: Beiträge zur Ätiologie und Klinik der schweren Formen angeborener und erworbener Schwachsinnszustände. Monogr. a.d. Grenzgebiet d.Neurol. & Psych. Nos. 23-25, 1921.

28. Dollinger, A.: Geburtstrauma und Zentralnervensystem. Ergeb. inn. Med. 31:373, 1927.

29. Ehrenfest, H.: *Birth injuries of the child* (new rev. ed.) New York: Appleton, 1931.

30. Eichhorst, H.: Über Veränderungen der Hypophysis cerebri bei Kretinismus und Myxödem. Deutsches Arch. Klin. Med. 124:207, 1917.

31. Finkelstein, H.: *Die durch Geburtstraumen hervorgerufenen Krankheiten des Säuglings*. Berlin: Fischer Verlag, 1902.

32. Finkelstein, H.: *Säuglingskrankheiten* (4th ed.) Amsterdam: Elsevier, 1938.

33. Fischer, B.: Das Geburtstrauma in seinen Folgen für Gehirn und Säugling. Schweiz. med. Woch. 54:905, 1924.

34. Fischer, J.: *The Labyrinth*. New York: Grune & Stratton, 1950.

35. Förster, O.: Zur Analyse und Pathophysiologie der striären Bewegungsstörungen. Ztschr. f. d. ges. Neurol. & Psychiat. 73:1, 1921.

36. Ford, F. R.: Cerebral birth injuries and their results. Medicine 5:121, 1926.

37. Ford, F. R.: *Diseases of the Nervous System in Infancy, Childhood and Adolescence* (3rd. ed.) Springfield, Ill.: Charles C. Thomas, 1952.

38. Ford, F. R., Crothers, B., and Putman, M.G.: *Birth Injuries of the Central Nervous System*. Medicine, Monograph No. 97. Baltimore, Williams & Wilkins, 1927.

39. Eröding, C. A.: Le nerf auditif et les lésions intracraniennes produit par l'accouchement chez le nouveau-né. Acta oto-laryng. 13:489, 1929.

40. Galebsky, A.: Vestibular nystagmus in newborn infants. Acta oto-laryng. 11:409, 1927.

41. Gurdjian, E. S., and Webster, J. E.: *Head Injuries*. Boston: Little, Brown & Co., 1958.

42. Guttner, M.D.: Über das Verhalten der Blutzirkulation des Fetus in der Geburt. Arch. Gynaek. 149:70, 1932.

43. Henkel, M.: Über intrakranielle Blutungen Neugeborener. Zentralbl. Gynaek. 46:129, 1922.

44. Hill, T. D., and Parr, G. (eds.): *Electroencephalography: A Symposium on its Various aspects*. New York: Macmillan, 1950.

44 a. Holland, E.: Fetal intracranial hemorrhage during birth. Brit. med. Journ. 1:868, 1920.

45. Holland, E.: Birth injury in relation to labor. Amer. J. Obst. & Gynec. 33:1, 1937.

46. Hughes, J. G., Ehemann, B., and Brown, U. A.: Electroencephalography of the newborn. Am. J. Dis. Children 76:620, 1948.

47. Hughes, J. G., Ehemann, B., and Brown, U. A.: Encephalography of the newborn: Abnormal encephalograms of the neonate. Am. J. Dis. Chil. 76:634, 1948.

48. Hughes, J. G., Ehemann, B., and Brown, U. A.: Electroencephalography of the newborn: Brain potentials of babies born of mothers given Seconal sodium. Am. J. Dis. Child. 76:626, 1948.

49. Hughes, J. G., Ehemann, B., and Hill, F. S.: Electroencephalography of the newborn: Studies on normal, full term infants while awake and while drowsy. Am. J. Dis. Child. 77:310, 1949.

50. Hughes, J. G., Hill, F. S., Green, C. R.: and Davis, B. C.: Electroencephalography of the newborn: Brain potentials of babies of mothers given Demerol, Delvinal sodium or morphine. Am. J. Dis Child. 79:998, 1950.

51. Kelemen, G.: Die Widerstandsfähigkeit des neugeborenen Felsenbeins gegenüber Traumen. Monatsschr. Ohrenh. 12:1496, 1935.

52. Kleitman, N., and de Kleyn, A.: The influence of asphyxia on vestibular nystagmus and an attempt to localize the seat of this influence in the reflex arc. Amer. J. Physiol. 69:160, 1924.

53. Kutvirt, O.: Über das Gehirn Neugeborener und Säuglinge. Beitr. prakt. u. theoret. Hals-Nasen-Ohrenh. 4:166, 1911; 5:249, 1912.

54. Labbé, R.: Surdi-mutité. Considérations sur l'étiologie et la pathologie. Arch. méd. d'ent. 41:257, 1938.

55. Lawrence, M. M., and Feind, C. R.: Vestibular response to rotation in newborn infants. Pediatrics 12:309, 1953.

56. Lubarsch, O.: Zur Kenntnis der im Gehirnanhang vorkommenden Farbstoffablagerungen. Berl. klin. Woch. 54:63, 1917.

57. Magnus, R. and de Kleyn, A.: Die Abhängigkeit des Tonus der Extremitätenmuskeln von der Körperstellung. Arch. f. ges. Physiol. 145: 534, 1912.

58. Magnus, R. and de Kleyn, A.: Experimentelle Physiologie des Vestibular-apparates bei Säugetieren mit Ausschluss des Menschen, in *Handbuch der Neurologie des Ohres*. Berlin: Urban & Schwarzenberg, 1924, Vol. 1 pp. 465-552.

59. Metzger, E.: Geburts-traumatische Veraenderungen am Auge: Tierexperimentelle Untersuchungen. Deutsche med. Woch. 51:1446, 1925.

60. Meyer, L. F.: *Krankheiten des Säuglingsalters*. Leipzig: G. Thieme, 1924.

61. Munro, D.: Cranial and intracranial damage in newborn: End-result study of 117 cases. Surg., Gynec. & Obstet. 47:622, 1928.

62. Naujoks, H.: *Die Geburtsverletzungen des Kindes*. Stuttgart: Verlag Enke, 1934.

63. von Pfaundler, M.: Studien über Frühtod, Geschlechtsverhältnis und Selektion zur intrauterinen Absterbeordnung. Ztschr. Kinderh. 57:185, 1935.

64. von Pfaundler; M.: Studien über Frühtod, Geschlechtsverhältnis und Selektion. II. Zum perinatalen Sterben: Die Totgeburten. Ztschr. Kinderh. 60:476, 1936.

65. von Pfaundler, M.: Studien über Frühtod, Geschlechtsverhaltnis und Selektion. III. Zum perinatalen Sterben: Die Neugeborenensterblichkeit. Ztschr. Kinderh. 62:351, 1940-1941; 63:1, 1942-43.

66. Pinhard, H.: *Nachuntersuchung geburtstraumatisch geschädigter Kinder*. Frankfurt am Main: 1928. (Inaugural Dissertation).

67. Preyerchtel, A.: Inner ear and cerebellar changes in pathological and fetal position: Their significance for static disturbances in earliest periods of life and for some anomalies of speech. Laryngoscope 39:421, 1929.

68. von Reuss, A.: Die Krankheiten des Neugeborenen, in *Enzyclopädie der klin. Medizin*. Berlin: J. Springer, 1914, speziller Teil, p. 187.

69. Ricker, G. and Regenslanz, P.: Beiträge zur Kenntnis der örtlichen Kreislaufstarrungen. Virch. Arch. path. Anat. 231:1, 1921.

70. Roberts, M. H.: The spinal fluid in the newborn, with especial reference to intracranial hemorrhage. J.A.M.A. 85:500, 1925.

70a. Roberts, M. H. Intracranial Hemorrhage in the newborn J.A.M.A., 113:280, 1939.

71. Ross, I.: *Klinische Untersuchungen an Frühgeburten mehrere Jahre nach der Geburt*. Frankfurt am Main: 1928. (Inaugural Disseration.)

72. Saenger, H.: Uber die Entstehung intrakranieller Blutungen beim Neugeborenen. Arch. Gyn. 120:294, 1923.

73. Saenger, H.: Uber die Entstehung intrakranieller Blutungen beim Neugeborenen. Monatschr. Geburtsh. and Gynäk. 65:251, 1924.

74. Schwitt, P.: Hypophysenuntersuchungen bei kongenitaler Lues. Centralbl. allg. Path. u. path Anat. 34:466, 1924.

75. Schur, E.: Studien über das statische Organ normaler Säuglinge und Kinder. Ztschr. Kinderh. 32:227, 1922.

76. Schwartz, Ph.: Die Ansaugungsblutungen im Gehirn Neugeborener. Ztschr. f. Kinderh., 29:102, 1921.

77a. Schwartz, Ph.: Die traumatische Gehirnerweichung des Neugeborenen. Ztschr. f. Kinderh. 31:51, 1922.

77b. Schwartz, Ph.: Erkrankungen des Zentralnervensystems nach traumatischer Geburtsschädigung. Ztschr. f. Neur. Psychiat. 90:263, 1924.

77c. Schwartz, Ph.: Die geburts-traumatische Schädigung des Kopfes Neugeborener und ihre Bedeutung für die Pathologie. Monatschr. f. Kinderh., 34:511, 1926.

77d. Schwartz, Ph.: Die traumatischen Schädigungen des Zentralnervensystems durch die Geburt. Anat. Untersuchungen Ergebn. Inn. Med. u. Kinderh., 31:165, 1927.

77e. Schwartz, Ph.: Geburtshilfe und Hirnschadigungen durch die Geburt. Zentralbl. f. Gynäk., 52:2116, 1928.

77f. Schwartz, Ph.: Birth injury as a cause of "status marmoratus" Archives of Pediatrics, Vol. 75, No. 2, February, 1958.

77g. Schwartz, Ph.: Virchow's congenital encephalomyelitis of the newborn. Archives of Pediatrics, Vol. 75, No. 5, May, 1958.

77h. Schwartz, Ph.: Birth injuries of the newborn. Investigations into their morphology, pathogenesis, clinical pathology and prevention. Monograph to be published.

78. Schwartz, Ph.: and Berberich, J.: Experimentelle Untersuchungen zur Frage der Geburts-traumas. Centralbl. allg. Path. 34:621, 1923-24.

79. Seitz, L.: Das spätere Schicksal der Kinder nach operativer Geburt. Arch. Frauenk. u. Eugenik 8:185, 1922.

80. Seitz, L.: Uber Hirndrucksymptome bei Neugeborenen infolge intracranieller Blutungen und mechanischer Hirnstörung. Arch. Gynäk. 82:328, 1907.

81. Seitz, L.: Uber Lokalisation und klinische Symptome intrakranieller Bluterguss Neugeborenen. Munch. Med. Wchnschr. 55:608, 1908.

82. Seitz, L.: Uber die Genese intrakranieller Blutungen bei Neugeborenen. Zentralbl. Gynäk. 36:1, 1912.

83. von Sicherer: Ophthalmoskopishe Untersuchungen Neugeborener. Verhandl. Ophth. Gesellsch. 34:201, 1907.

84. Siegmund, H.: Neue Untersuchungen über Virchows Encephalitis interstitialis congenita. Klin. Wchnschr. 1:2274, 1922.

85. Siegmund, H.: Geburtsschädigungen des kindlichen Gehirns und ihre Folgen. Munch med. Wchnschr. 70:137, 1923.

86. Siegmund, H.: Die Entstehung der Porencephalien und Sklerosen aus geburtstraumatischen Hirnschädigungen. Virchows Arch. path. Anat. 241:237, 1923.
87. Simmonds, M.: Über syphilitische Erkrankungen der Hypophyse, insbes. bei Lues congenita. Dermat. Wchnschr. 58:194, 1914.
88. Simmonds, M.: Atrophie des Hypophysenvorderlappens und hypophysäre Kachexie. Deutsche med. Wchnschr. 55:441, 1918.
89. Simmons, M.: Zur Pathologie der Hypophyse. Verhandl. deutsch. path. Gesellsch. 1924.
90. Staemmler, M.: Über den Befund von Fettkörnchenzellen im Gehirn neugeborener Tiere. München. med. Wchnschr. 70:1430, 1923.
91. Stern, A.: Die Bedeutung der Kindlichen Geburtsverletzungen für die Geburtschilfe. Arch. Gynäk. 124:44, 1925.
92. Thielemann, R.: Zur Frage der Geburtsschädigung des Gehörorgans. Folia oto-laryng. 15:126, 1927.
93. Thornval, A.: L'épreuve calorique chez les nouveau-nés. Acta oto-laryng. 2:451, 1920-21.
93a. Thornval, A.: Die kalorische Reaktion bei Neugeborenen. Zentralbl. ges. Neurol. u. Psychiat. 25:411, 1921.
94. Virchow, R.: Kongenitale Encephalitis und Myelitis. Virchows Arch. path Anat. 38:129, 1867.
95. Virchow, R.: Encephalitis congenita. Berl. klin. Wchnschr. 20:705, 1883.
96. Voss, O.: Die Symptomatologie des Geburtstraumas. Klin. Wchnschr. 2:854, 1923.
97. Voss, O.: Geburtstrauma und Gehörorgan. Ztschr. Hals-Nasen-u. Ohrenh. 6:182, 1923.
98. Voss, O.: Klinisch und pathologisch-anatomische Folgeerscheinungen geburtstraumatischer Schädigungen des Felsenbeins. Monatsschr. Kinderh. 34:568, 1926.
99. Voss, O.: Die Symptomatologie des Geburtstraumas, in *Tagung der deutschen Kinderärzte in Düsseldorf*, 1926.
100. Voss, O.: Geburtstrauma und Gehörorgan. Acta oto-laryng. 11:73, 1927.
101. Wahl, A.: Systematische Untersuchungen über geburtstraumatische Veränderungen der basalen Ganglien bei Neugeborenen und Säuglingen und ihre Bedeutung für die sogenannten angeborenen Erkrankungen der basalen Ganglien. Ztschr. Kinderh. 49:372, 1930.
102. Warwick, M.: Necropsy findings in newborn infants. Am. J. dis. Child. 21:488, 1921.
103. Wiechers, A.: Geburtsschädigungen des Gehirns und Pathologie des frühen Kindesalters. Med. Klin. 21:1646, 1925.
104. Winnewisser, A.: Ein Beitrag zur Frage der Geburtsschädigung Taubstummer. Arch. Ohren-, Nasen- u. Kehlkopfh. 146:261, 1939.
105. Wolpert, I.: Über den Fussohlenreflex der Säuglinge. Deutsche Ztschr. Nervenh. 89:98, 1926.
106. Ylppö, A.: Zur Physiologie, Klinik und zum Schicksal der Frühgeborenen. Ztschr. Kinderh. 24:1, 1920.
107. Ylppö, A.: Das Wachstum der Frühgeborenen von der Geburt bis zum Schulalter. Ztschr. Kinderh. 24:111, 1920.
108. Ylppo, A.: Einige Kapitel aus der Pathologie der Frühgeborenen Kinder. Klin. Wchnschr. 1:1241, 1922.
109. Ylppo, A.: Zum Entstehungsmechanismus der Blutungen beim Frühgeborenen und Neugeborenen. Ztschr. Kinderh. 38:32, 1924.

784 Park Avenue, New York City, 21

Electrophoretic Studies of Serum Proteins in Nutritional Edema in Egyptian Children

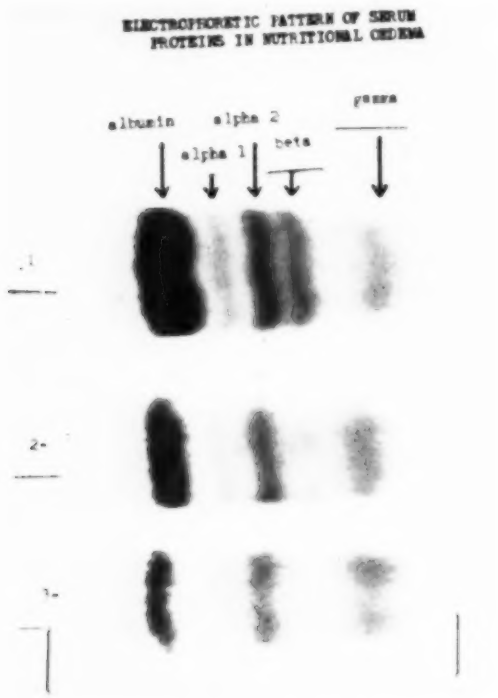
S. Awwaad, D.C.H., M.D.Ch.* and
E. M. Abdel-Wahab, Ph.D., D.M.Sc.*
Egypt

Studies on nutritional edema in Egyptian infants and children[1,2] have revealed that the condition is clinically and pathologically identical with what is called "Kwashiorkor syndrome". According to the FAO/WHO Expert Committee on Nutrition 1953, this syndrome is the result of protein malnutrition *i.e.*, of relative deficiency of protein food stuffs in the diet (Brock *et al.*, 1955)[4]. Consequently, a diminution of blood proteins would be most expected in such a condition. Besides it has been shown that the liver in these cases constantly shows a marked degree of fatty change, and as the liver plays a fundamental role in the synthesis and metabolism of blood proteins, it is very likely that such an extensive parenchymatous damage may seriously interfere with its proper function in this respect.

Although the literature on the subject of serum proteins is quite voluminous, there is less information on this subject in Kwashiorkor. Williams[5] has summarised the findings of Dean and Schwartz regarding the serum proteins of Kwashiorkor as follows: "In the serum, the total proteins and albumin are considerably below normal, and the globulin is high. The height of the globulin at the start and at the end of treatment are both due to γ globulin; the α and β globulins are less affected. With treatment, the albumin rises more than the total globulins so that the AG. ratio rises, but it seldom goes above unity". Recently Snyderman[6] also reported that a depression in the concentration of serum albumin and a rise in the globulin, mainly involving the α and β fractions, occur in Kwashiorkor. On the other hand Zeldis *et al.*[7], experimenting on dogs, found that the long continued reduction of dietary protein results in a striking decrease in the plasma albumin while the total globulin is

* Pediatric and Clinical Pathology Departments, Ein Shams University, Cairo, Egypt.

slightly decreased. In man, Beiler, Echer and Spies[8] found that an inadequate protein intake leads to reduction of both albumin and globulin fractions with a proportionately greater decrease in albumin. Seibert and Nelson[9] reported that the γ globulin seems to be the most refractory to inanition diminution.



1. The pattern in a normal child. 2 & 3. The pattern in two cases of nutritional oedema.
Note: I. The marked reduction in the albumin. II. The marked reduction in the β fraction. III. The rise in the γ-fraction.

The scantiness of the literature on this subject together with the diversity of the results reported by different authors have stimulated us to study this problem, using the technique of electrophoresis on paper, which is supposed to give the most accurate information about the serum proteins.

CLINICAL MATERIAL

Thirteen normal children between 1 and 3 years of age were collected. Determinations of their serum proteins were carried out and the results obtained served as a basis for comparison with the results obtained in the diseased cases.

Twenty-four cases of nutritional edema were subsequently collected and investigated. All of them were suffering from edema of varying degrees of severity. Six of these were advanced cases showing the skin and hair lesions typical of Kwashiorkor. Clinical examination of the heart and chest, in all cases, revealed normal findings. The liver was moderately enlarged in 14 cases, markedly enlarged in 3, and normal in the remaining 7. The spleen showed mild enlargement in 4 cases only. None had ascites or dilated veins of the abdominal wall. In all cases, the urine was free from albumin, casts and Bilharzia ova, and the stools were negative for parasites and ova.

After being investigated the cases were treated with high protein diet, repeated plasma transfusions and sufficient vitamins.

Determination of serum protein fractions was done for all cases on admission and was subsequently repeated in 5 cases after the subsidence of edema and 1 to 3 weeks later. Liver puncture biopsy was performed in 10 cases on admission and was repeated in the above mentioned 5 cases with each estimation of serum protein fractions.

BIOCHEMICAL METHOD

Venous blood specimens were obtained with a minimum of stasis and were allowed to clot. The serum was withdrawn on the same day, samples showing any trace of hemolysis being rejected. Most of the samples were analyzed on the same day. A few were frozen at -4°C. to be analyzed on the next day.

The total protein concentration was estimated using the biuret method. Electrophoresis was carried out on Whatman No. 1 filter paper at pH 8.6 in an M/10 barbitone buffer (Abdel-Wahab, Rees and Laurence, 1956)[10]. By means of a glass slide 0.01 ml of serum was applied to the paper strip 10 cm from its cathodic end. A potential of 100 volts was applied to the paper for 20 hours. The strips were then dried in an oven at 120°C for 30 minutes, and stained for 10 minutes in 0.2% lissamine green S.F. 150 (I.C.I. dyestuff) in 15% acetic acid (Abdel-Wahab and Laurence,)[11]. Wash-

Table I—Normal Values for Children 1-3 Years:

No.	Sex	Age in mons.	Wgt. kg.	Total protein g %	Alb. g %	Globulins g %				Total Glob. g %	A/G ratio
						α_1	α_2	β	γ		
1	M	16	11.00	7.4	3.80	0.32	0.84	0.84	1.53	3.54	1.09
2	M	19	11.00	7.5	4.15	0.31	1.14	0.75	1.15	3.35	1.24
3	M	21	11.00	7.5	4.77	0.17	0.68	0.69	0.99	2.53	1.88
4	M	23	9.75	6.1	4.28	0.33	0.92	0.92	1.65	3.82	1.12
5	F	23	10.25	7.0	4.59	0.20	0.67	0.57	1.07	2.41	1.90
6	M	24	11.00	6.9	3.92	0.20	0.65	0.73	1.10	2.68	1.32
7	M	24	11.50	7.5	4.88	0.23	0.81	0.89	0.99	2.92	1.68
8	M	24	12.00	6.9	3.99	0.24	1.02	0.52	1.13	2.91	1.36
9	M	24	11.00	7.4	4.56	0.25	0.95	0.59	1.05	2.85	1.60
10	M	24	10.4	7.5	4.59	0.26	1.01	0.57	1.16	3.00	1.29
11	F	30	12.00	7.5	4.59	0.26	1.06	0.70	1.02	2.98	1.52
12	M	30	13.75	7.9	4.83	0.29	0.72	0.64	1.63	3.37	1.34
13	F	36	14.00	6.2	4.45	0.21	0.80	0.73	0.71	2.45	1.81
	Average values			7.37	4.37	0.25	0.90	0.70	1.17	3.00	1.40

Table II—Clinical Data and Serum Protein Pattern in Cases of Nutritional Edema.

No.	Sex	Age mons.	Wt. kg.	Degree of* edema	Liver enlargement	Total Bld.prot. g. %	Electrophoresis g %				Total Glob. g.%	A/G Ratio
							Alb.	α_1	α_2	β	γ	
1	M	14	7.8	+	+	4.6	2.09	0.28	0.49	0.39	1.35	2.51	0.83
2	F	15	7.3	++	+	4.9	2.98	0.44	0.69	0.44	1.25	2.82	0.74
3	M	17	9.0	+++	-	4.6	1.36	0.32	0.92	0.42	1.58	3.24	0.42
4	M	15	8.7	++	+	4.4	2.26	0.35	0.44	0.36	0.79	2.14	1.06
5	M	18	7.4	++	+++	4.5	2.71	0.11	0.51	0.27	1.21	1.09	1.43
6	F	18	9.0	++++	-	3.4	1.16	0.30	0.50	0.34	1.10	2.24	0.52
7	F	18	9.5	++++	+	3.4	1.18	0.29	0.74	0.38	0.84	2.23	0.51
8	F	20	8.6	++	+	4.3	2.13	0.22	0.39	0.39	1.22	2.20	0.95
9	F	20	7.8	++++	+	4.0	2.00	0.24	0.57	0.24	0.95	2.00	1.00
10	M	24	9.5	++	-	4.2	2.43	0.19	0.23	0.20	1.15	1.77	1.37
11	M	24	10.2	++++	+	4.7	1.43	0.33	0.44	0.44	2.06	3.27	0.44
12	F	24	8.5	++	+	4.2	1.99	0.24	0.51	0.39	1.09	2.21	0.90
13	F	24	8.4	++	-	4.6	1.32	0.17	0.69	0.51	1.91	3.28	0.40
14	F	24	7.9	+++	+	5.3	2.58	0.21	0.69	0.45	1.36	2.71	0.96
15	M	25	9.5	++	+++	4.4	1.60	0.36	0.70	0.42	1.32	2.80	0.57
16	M	27	11.6	+++	++	4.2	1.35	0.24	0.92	0.30	1.39	2.85	0.47
17	F	28	10.4	++	+	4.0	2.30	0.12	0.41	0.23	0.94	1.70	1.35
18	M	30	12.5	+++	+	4.1	1.31	0.14	0.28	0.70	1.67	2.79	0.47
19	M	30	8.8	++++	-	4.9	2.20	0.20	0.49	0.42	1.69	2.70	0.82
20	M	30	9.5	++	+	5.6	3.53	0.17	0.46	0.39	1.05	2.07	1.71
21	M	34	12.2	++	+	5.5	2.22	0.27	0.58	0.50	1.93	3.28	0.69
22	M	34	8.6	++	-	4.6	1.77	0.21	0.56	0.33	1.11	2.23	0.79
23	F	36	10.0	++++	+	3.2	1.40	0.25	0.37	0.29	0.89	1.80	0.78
24	M	36	12.0	++++	+++	4.2	1.14	0.24	0.87	0.47	1.48	3.06	0.37
Average values						4.99	1.96	0.249	0.56	0.41	1.34	2.55	0.75

* Edema + , limited to dorsum of hands and feet
++ , extending to knees
+++ , generalized edema involving all limbs and the face
++++, more severe grade of edema, causing rupture of the epidermis in certain areas of the lower limbs and buttocks, with exposure of red and oozing surfaces

ing was continued with 2% acetic acid in tap water until the background of the strip was white. Three successive washes, each for 2 minutes, were usually required. The lissamine green stain was preferred because of the ease with which the background can be cleared, the inexpensiveness of the washing fluid, and the ease of elution of the dye. The electrophoretic pattern was cut into pieces, each containing one of the protein fractions. Each band was eluted in 10 ml phosphate buffer, pH 6.0 and the resulting colour was read in an Evelyn photoelectric colorimeter using a 635 (red) filter.

RESULTS

1. *Biochemical Investigations*: The figures obtained are tabulated as follows: Normal values for children between 1 and 3 years are given in Table I, and clinical data and results obtained in cases of nutritional edema in Table II. Table III shows the serum protein pattern of five of these cases when first seen and also after clinical disappearance of the edema.

Table III—Serum Protein Fractions in Cases of Nutritional Edema Before and After Clinical Cure of Edema

Case No.	Stage	Total protein g %	Alb. %	Globulins				Total glob. g %	A/G ratio
				α1	α2	β	γ		
5	Before	4.6	2.71	0,11	0.31	0.27	1.99	1.89	1.43
	During	4.9	2.29	0.32	0.56	0.56	1.17	2.61	0.88
	After	6.9	2.85	0.41	1.00	0.90	1.40	4.01	0.70
14	Before	5.3	2.59	0.21	0.69	0.45	1.36	2.71	0.96
	After	7.9	4.02	0.25	0.87	1.09	1.64	3.88	1.03
18	Before	4.1	1.31	0.14	0.28	0.70	1.67	2.79	0.47
	After	6.7	2.26	0.49	0.68	0.79	2.48	4.44	0.51
19	Before	4.9	2.20	0.20	0.49	0.32	1.69	2.70	0.82
	After	6.7	2.75	0.50	0.71	0.75	1.21	3.95	0.69
20	Before	5.6	3.53	0.17	0.46	0.39	1.05	2.07	1.71
	After	6.9	3.69	0.27	0.87	1.09	1.65	3.87	0.95

From the foregoing tables it is seen that:

I - In Normal Cases between 1-3 yrs

(Table I) the average values for total serum proteins, serum albumin, α1, α2, β & γ globulins are found to be 7.37, 4.37, 0.25, 0.88, 0.70, 1.17 g. % respectively.

From the foregoing tables it is seen that:

I. In Normal Cases between 1-3 yrs. (Table I) the average values for total serum proteins, serum albumin, α1, α2, β & γ globulins are found to be 7.37, 4.37, 0.25, 0.88, 0.70, 1.17 g. % respectively.

II. *In Cases of Nutritional Edema (Table II)*

1. There is a constant and marked diminution in the total proteins. The values ranged between 3.2 and 5.6 with an average of 4.90 g%.
2. The reduction was constant and most marked in the albumin fraction (fig. 1) where the values ranged between 1.14 & 3.53, with an average of 1.80 g%.
3. The total globulin concentration, on the other hand, was not uniformly affected. It was reduced in 19 out of the 24 cases studied, while in the remaining 5 cases, it was either normal or slightly elevated. However, the average for the whole group was about 14% below the average for normal cases.
4. Concerning the globulin fractions, (fig. 1):
   i — The β-globulin showed a constant and marked reduction and its average figure in the whole group was about 50% less than the normal.
   ii — The α_1 and α_2 fractions showed a less constant and less marked reduction.
   iii — The γ globulin, on the other hand, was on the high side of normal or showed slight elevation.
5. Consequently, the A/G ratio was in the majority of cases (18 out of 24) below 1.0, which is considered the threshold for normality (Abdel-Wahab *et al.*)[10]

III. — In the Group in which the determinations of serum proteins were repeated after subsidence of edema.

1. The previously lowered total proteins and albumin showed a constant rise. However, clinical disappearance of the edema was not accompanied by complete return of these levels to normal.
2. The α_1 and α_2 globulins tended to return to normal levels.
3. The β fraction also tended to return to normal and even became higher in some cases.
4. The γ fraction, on the other hand, showed a constant rise even in the cases where it was originally high.

5. Consequently, the total globulin concentration showed a constant rise but, in the majority of cases, it was noticed that the A/G ratio remained below unity.

II.—Liver Puncture Biopsies:

It was found that cases of nutritional edema constantly show a marked degree of fatty change of the liver cells, with patchy necrosis in the more severe cases and proliferation of the portal tracts in the more chronic ones. The subsidence of edema was associated with a marked improvement of the fatty change. However, a slight degree of fatty change was still present in the cases followed 2-3 weeks after subsidence of the edema.

DISCUSSION

I.—Comparing our results with those reported in the literature, it could be noticed that:

1. The marked and constant diminution obtained in the values for the total serum protein and for albumin is in agreement with the previous results.
2. The common (75%), though less remarkable reduction (14%) obtained in the globulin concentration does not agree with the results obtained by Dean and Schwartz and also differs from the recent report given by Snyderman. However, they agree with the findings of Bieler, Ecker and Spies in man, and those of Zeldis *et al* in experimental animals.
3. The constant and marked diminution which we observed in the β fraction in the present series, has not, to our knowledge, been previously reported by other workers.
4. The tendency for the γ globulin to remain unreduced or even to become elevated in cases of protein deficiency was commented upon by Dean and Schwartz, Snyderman, and Siebert & Nelson, but its constant rise after clinical cure was only reported by Dean and Schwartz.
5. The increase of the protein fractions with subsidence of the edema is not a reflection of decreased plasma volume, as in edema the interstitial fluid is increased but the plasma volume is often reduced[12], and also because the decrease in the protein fractions with edema and the increase after its subsidence do not involve all fractions equally (Table III).
6. Our observation that the A/G ratio is usually below unity,

before as well as after treatment is also in agreement with the findings of Dean and Schwartz.

II. —From Tables II & III it is evident that the degree of edema does not always parallel the degree of hypo-alubuminemia. (Compare case 1 with case 14, 9 with 15 and 18 with 19 in Table II and case 5 after subsidence of edema with case 20 before treatment in Table III). This observation supports the recent concept that though hypo-albuminemia and nutritional edema always co-exist, yet the former is not the sole causative factor for the latter and that other factors must have a closer causative relationship. Among these other factors Gallon[13] has mentioned the low rate of blood flow and the reduced oxygen saturation and content in the venous blood.

III. —The fact that 2-3 weeks after subsidence of edema some fatty changes in the liver cells still exist and some diminution in the total proteins and the albumin levels persists shows that the liver condition is the causative factor for delay in the return of blood proteins to normal levels. Unfortunately, the relatives of the patients usually insisted on the discharge of the children immediately after the disappearance of the edema and before we could establish the time requird for these values to return to normal.

IV. —The constant and marked reduction which is observed in the albumin and the β globulin in diseased cases, and their tendency to return to normal with improvement of the liver condition, supports the belief that the liver is the chief source of albumin and β globulin.

V. —The constant rise of γ globulin to above normal observed in the recovering cases in spite of the improvement in the liver condition as shown by liver puncture biopsy, is against Martin's hypothesis[14] that the liver normally destroys γ globulin. If this were the case the γ globulin level should drop with the improvement of liver condition, instead of rise. However, the cause for this rise has still to be found.

SUMMARY AND CONCLUSIONS

1. The changes which occur in the electrophoretic pattern of serum proteins in nutritional edema have been studied. A constant and marked reduction in the total proteins, as well as in the albumin

and the β globulin fraction was noted, while the α_1 and α_2 globulin fractions were less frequently affected. On the other hand, the γ globulin continued to be normal or became moderately elevated (fig. 1).

2. With the clinical disappearance of the edema the reduced levels tended to return to normal while the γ globulin continued to rise.
3. The results obtained are discussed and compared with similar data reported by other authors.
4. Our results support the recent concept, that although hypoalbuminemia and nutritional edema always co-exist, the former could not be considered as the sole causal factor for the latter.
5. On the other hand, our results do not support Martin's hypothesis that the liver normally destroys the γ globulin fraction.

REFERENCES

1. Shukry, H. Awwaad, S. and Hashem, M., Gaz. Egypt. Ped. Ass., 1:1, 1952.
2. Alti, O., *Ibid.*, 4:140, 1956.
3. Awwaad, S. and Attia, O., Unpublished data.
4. Brock, J. F., Hansen J. P. L., How, E. E. Pretorius, P. J., Davel, J. G. A. and Hendrickse, R.J.: Lancet, 2:335, 1953.
5. Williams, C. D., J. A. M. A., 153:1280, 1953.
6. Snyderman, S. E., Pediatrics, 21:117, 1958.
7. Zeldis, L. J., Alling, E., McGeord, A. B. and Kulka, J. P., J. Exp. Med., 82:137, 1945.
8. Bieler, M. M., Ecker, E. E. and Spies, T. D., J. Lab. & Clin. Med., 32:150, 1947.
9. Seibert, F. B. and Nelson, J. W., Am. Rev. Tub., 47:66, 1943.
10. Abdel-Wahab, E. M., Rees, V. H. and Laurence, D. J. R., Ciba Foundation Symposium on Paper Electrophoresis, London, 50, 1956.
11. Abdel-Wahab, E. M. and Laurence, D. J. R., Biochem. J., 60:XXXV, 1955.
12. Holliday M. and Egan Th.J., Ped. clinics North America, 6:89, 1959.
13. Galbut, F., J. Clin. Invest., 27:352, 1948.
14. Martin, N. H., Brit. J. Exp. Path., 30:231, 1949.

A New Treatment for Seborrhea Capitis in Infants and Children

J. R. Kabel, M.D.* and A. Nalmabadi, M.D.**

While the etiology of seborrheic dermatitis has not been fully established, it is generally regarded as an inflammatory process related to a dysfunction and/or overactivity of the sebaceous glands. In turn the pilo-sebaceous apparatus may be overstimulated by an excessive activity of the androgen-producing glands of internal secretion. Furthermore, it is generally acknowledged that genetic and metabolic factors are involved. In the ordinary forms of seborrhea capitis infantum, there may also be a faulty or excessive keratinization of the horny layers of the scalp. As this substrate of lipids and proteins accumulates, invading microorganisms find an almost ideal culture medium and normally inactive saprophytes become active parasites with pathogenetic effects[1]. The organisms most commonly isolated in seborrheic eruptions are the pityrosporon of Malassez, Staphlococcus albus, S. aureus and Streptococcus pyogenes.[2] Chemical decomposition of the excessive secretions takes place rapidly which in turn may give rise to a severe sensitization of the scalp.

Seborrhea capitis, especially the dandruff or "sicca" type probably affects almost everyone to some extent. According to Finnert,[3] it has been estimated that 25% of all dermatologic patients seen in private practice suffer with seborrheic disturbances which make dandruff, seborrhea oleosa and seborrheic dermatitis of considerable quantitative importance to the physician.

Witten and Sulzberger[4] have stated that care of the scalp should be considered a prophylactic procedure, not unlike brushing the teeth, and should be done regularly, thoroughly and "forever."

Frequently this "forever" part of the problem starts in infancy with the onset of scalp seborrhea or "cradle cap." This involvement is characterized by thick, yellowish greasy scales of the vertex and possibly covering most of the scalp. In many cases the hair may be matted with crusts. This crust or cap may vary in color, as

* Elizabeth, N. J.
** Babies Hospital, Newark, N. J.

James[5] has pointed out, but frequently has a dirty waxy appearance. It is a most distressing cosmetic and therapeutic problem.

In older children seborrheic dermatitis is much less common than in adults. However, the condition is sometimes seen and, in general, the scaling will be dry (pityriasis sicca) or oily (pityriasis oleosa[6]).

Since there is no "cure" for seborrhea, treatment should be aimed at the most effective method that will achieve symptomatic relief as rapidly as possible. Therapy then must encompass the following factors:

1. Effective means of removal of scales and crusts with mechanical cleansing and clearing of scalp oiliness.
2. An anti-pruritic modality in order to prevent aggravation of the condition by scratching.
3. Activation of the healing process with stimulation of the growth of healthy tissue.
4. An antimicrobial agent of sufficiently broad spectrum.
5. A non-irritating, non-sensitizing and most important, a non-toxic preparation.

A rational approach to combine these aims of therapy seems to have been made in a new preparation* which contains 2% allantoin, 1% hexachlorophene, and 2% crude coal tar extract in a highly penetrating and greaseless base.

According to Payne,[7] the clinician may be well advised to attach almost as much importance to the choice of the vehicle for his remedy as to the choice of the remedy itself. This consideration is of particular importance in a therapeutic agent with the multiple functions listed above, and the carrier used in the new product seems to be eminently suited for this purpose.

Previous experience with a tar-allantoin combination and with hexachlorophene preparations gave us reason to expect a high degree of safety in use of the test cream. In our series of patients there were no instances of irritation, nor evidence of sensitization. The concentration of tar in the test preparation is only 2 percent. This is less than one-half that of the tar-allantoin lotion in regular use for scaling dermatoses; the latter preparation has been observed to be remarkably well tolerated.[8-11]

* Sebical Cream, supplied by Reed & Carnrick, Kenilworth, N. J.

As a part of the study, the effect of the vehicle alone was compared with the test preparation, using the "symmetrical paired comparison" technique of Sulzberger, Baer, Kanof and Lowenberg.[12] This is essentially a rapid screening procedure for evaluating topical medications. The vehicle (placebo) was used on one side of the head and the test preparation on the contralateral side, with the results as summarized in Table I.

TABLE I

CONTRALATERAL CONTROLLED STUDY OF TAR-ALLANTOIN-HEXACHLOROPHENE CREAM

Subject No.	Severity of Lesions before treatment	Severity after 1 week	
		Placebo Cream	Test Cream
1	5	4	1
2	5	5	0
3	4	5	1
4	4	3	0
5	5	4	1
6	5	5	1
7	4	3	0

KEY TO GRADING THE SEVERITY OF LESIONS:

0—No lesions.
1—No scaling, but some reddening delineating affected areas of hairy areas only.
2—Moderate scaling and redness of hairy areas only.
3—Moderate scaling and redness of the scalp with some extension to contiguous areas.
4—Less severe crusting, but with severe redness limited to hairy areas.
5—Severe crusting and erythema over most of the scalp and extending to adjacent areas.

The results of this screening procedure, which required a high degree of cooperation and care on the part of the mother, justified a full-scale trial of the medication.

METHOD

All patients were treated by first cleansing the scalp with warm water and soap. The cream was then applied, the amount used depending upon the area to be covered but sufficient to leave a soft moistened area. Application of the cream was advised three or four times daily and cleansing once daily during regular baths. The cream was used daily until the course of therapy was completed.

RESPONSE TO THERAPY

Thirty-two patients with cradle cap or associated seborrheic dermatitis were treated in this series. Many had been treated with the usual modalities with little or no response. In many of the children noted in Table 2 the response to therapy was dramatically

TABLE 2

RESULTS OF TREATMENT OF VARIOUS DERMATOSES WITH TAR-ALLANTOIN-HEXACHLOROPHENE CREAM

Patient	*Sex*	*Age*	*Diagnosis*	*Result*
T.R.	M.	7 mos.	Seborrhea Capitis	Completely cleared
P.G.	F.	2 mos.	" "	" "
D.S.	F.	4 mos.	" "	" "
P.D.	F.	16 mos.	" "	" "
P.B.	F.	6 mos.	" "	" "
P.H.	F.	8 mos.	" "	" "
A.M.	M.	11 mos.	" "	" "
L.F.	M.	14 mos.	" "	" "
R.P.	M.	9 mos.	" "	" "
L.S.	F.	8 mos.	" "	" "
V.R.	F.	10 mos.	" "	" "
B.W.	F.	4 mos.	" "	" "
R.L.	F.	20 mos.	" "	" "
M.B.	M.	2 yrs.	" "	" "
T.R.	M.	6 mos.	" "	" "
H.C.	M.	3 mos.	" "	" "
A.A.	F.	18 mos.	" "	" "
G.S.	F.	9 mos.	" "	" "
B.R.	M.	11 mos.	" "	" "
W.S.	M.	4 mos.	" "	" "
M.L.	F.	7 mos.	" "	" "
E.O.	F.	2 yrs.	Atopic Dermatitis	Improved
A.O.	M.	8 mos.	" "	" "
B.C.	M.	8 yrs.	" "	Improved
L.G.	F.	14 yrs.	" "	Poor
M.S.	M.	2 yrs.	" "	Improved
D.A.	F.	11 mos.	" "	Completely Cleared
J.L.	M.	9 yrs.	" "	" "
E.S.	M.	7 yrs.	" "	" "
N.R.	F.	16 mos.	" "	" "
A.R.	M.	10 yrs.	" "	" "
M.S.	F.	3 yrs.	" "	" "

prompt, sometimes with complete remission within a week or ten days. Classification of the therapeutic response as complete clearing indicates not only cessation of scaling but also elimination of any other evidence of the lesions. "Improved" indicates elimination of scaling but residual redness and the classification of poor or no relief is self explanatory.

From Table 2 it will be seen that there were 21 cases of seborrhea capitis in this study, all of whom cleared completely on the tar-allantoin-hexachlorophene cream. Of all 32 cases there were 27 who did respond to the point of complete clearing (84.42%). In

these 27 patients the duration of therapy ranged from less than 7 to 28 days.

In the patients who did not clear with the new cream, 4 showed improvement but not complete remission and one patient with atopic dermatitis was not benefitted. In the over-all group of patients with atopic dermatitis six patients cleared completely and four showed quite dramatic improvement.

SUMMARY

In the group of patients treated for seborrhea capitis or cradle cap all responded to therapy. We found this cream to be the most efficacious product we have encountered. It promptly eliminates scaling and just as promptly alleviates pruritus, a frequent and bothersome concomitant of the seborrhea. We also noted that in some atopic patients there was very prompt relief of the pruritus accompanying these lesions. Even in those atopics whose skin lesions did not clear there was a very dramatic relief of the itching. The preparation also brought minor secondary infections under control and microbial involvement did not occur in those cases where infection was not present at the start of therapy.

One outstanding advantage of this new cream is the simplicity offered in the control of these troublesome skin lesions without resorting to steroid therapy either internally or topically.

CONCLUSIONS

A new topical preparation (Sebical Cream) containing allantoin, hexachlorophene and crude coal tar extract, has been found exceptionally effective in the treatment of seborrhea capitis and other scaly lesions of the scalp.

REFERENCES

1. Behrman, H. T.: The Scalp in Health and Disease, P. 240, St. Louis, C. V. Mosby Co., 1952.
2. Mitchell-Heggs, G. B.: Modern Practice in Dermatology, P. 223, Butterworth & Co., London, 1950.
3. Finnerty, E. F.: New England Jour. Med. 255:614-616, 1956.
4. Witten, V. and Sulzberger, M.: Pediatric Clinics No. America, Aug. 1956, P. 719-749.
5. James, T.: So. African Medical Journal, 30:485-486, 1956.
6. Caspers, A. P.: Canadian Medical Journal, 79:113-118, 1958.
7. Mitchell-Heggs, G. B.: Modern Practice in Dermatology, P. 777, Butterworth & Co., London, 1950.
8. Welsh, A. and Eds, M.: Ohio State Med. Journ. 53:805-807, 1959.
9. Bleiberg, J. and Saltzman, J. A.: Clin. Med. 5:485-488, 1958.
10. Bleiberg, J.: Ann. New York Acad. Sc. 73:1028-1031, 1958.
11. Clyman, S. G.: Ann. New York Acad. Sc. 73:1032-1037, 1958.
12. Sulzberger, M. G., Baer, R. L., Kanof, A., and Lowenberg, C.: J. Invest. Dermat. 7:227, 1946.

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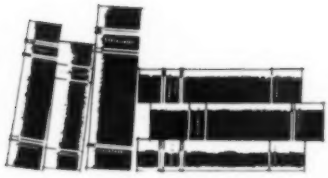

. . . Books

Edited by

MICHAEL A. BRESCIA, M.D.

THE HEINZ HANDBOOK OF NUTRITION, First Edition. Pages 425, cloth, McGraw-Hill Book Co., New York, 1959. Price $5.75.

The editorial board of H. J. Heinz Co. has compiled a one volume textbook on the science of nutrition. It is a comprehensive work on the principles of nutrition as applied to dietary practices and institutional dietetics, as well as on the role of nutrition in preventive and therapeutic medicine. The book is written in a concise and authoritative manner, with a clarity of expression and simple style for easy reading.

Part 1—The subject matter is organized as follows: Deals with the basic physiology and biochemistry of the human body as it relates to food intake and utilization.

Part 2—Presents the various nutrients, their sources, metabolism, physiology and interrelationships.

Part 3—Encompasses human nutritional requirements and nutrition under varying conditions of health and periods of physiologic stress.

Part 4—Devoted to nutrition in disease—the relationship between nutrition and specific diseases and the practical therapeutic and preventative aspects of special diets.

Part 5—Presents miscellaneous but essential aspects of nutrition not related to the first four divisions.

The manual represents and summarizes up-to-date accepted information, scientific and clinical thought on nutrition in health and in disease. Practical diets, charts and extensive tabular material are included in this volume thus placing valuable information at the fingertips of the busy practitioner. I recommend this valuable and practical handbook on nutrition to all physicians, nutritionists, dieticians, nurses and especially to the general practitioner.

JOSEPH M. COVELLI, M.D.

Authors' Summaries . . .

BURT, R. R.: Intestinal Polyps in Children. (Northwest Medicine 57:1004, August 1958).

It behooves all of us to search diligently for possible polyps in any child with blood in the stool, diarrhea, recurrent abdominal cramps or history of mass prolapsing from the anus. In addition to ordinary history and physical examination, sigmoidoscopy and contrast air study of the colon are necessary.

Some polyps will be passed spontaneously; this may account for inabiblity to find a polyp even though symptoms suggested its presence. However, only after repeated examinations should this assumption be made.

Isolated polyps within reach of the sigmoidoscope should be removed, when identified. The young child with several polyps in the colon above this level and with minimal symptoms may be observed for a year or so to determine if diffuse polyposis will develop requiring total colectomy rather than polypectomy.

Incidence of malignancy in adenomas increases at puberty. Therefore, definitive operation should be carried out before this age is approached.

BURNARD, E. D. AND CROSS, K. W.: RECTAL TEMPERATURE IN THE NEWBORN AFTER BIRTH ASPHYXIA. (British Medical Journal 5100:1197, Nov. 15, 1958).

Neonatal rectal temperature was measured at two-hourly intervals in 53 infants after normal delivery and in 15 after birth asphyxia. Asphyxia was found to cause a significantly lower temperature for 16 hours.

The same effect followed the maternal administration of pethidine independently of apnoea at birth.

The reduced temperature appears to be a natural consequence of anoxia in the baby.

KERR, M.R. AND DUNBAR, J. M.: TUBERCULOUS MENINGITIS FOLLOWING B.C.G. VACCINATION. (British Medical Journal 5103: 1019 Oct. 25, 1958).

A case of tuberculous meningitis is described occurring in an 11-months-old baby who had been given B.C.G. vaccine nine months previously. The infecting organism was shown to be a virulent strain of Mycobacterium tuberculosis of the human variety.

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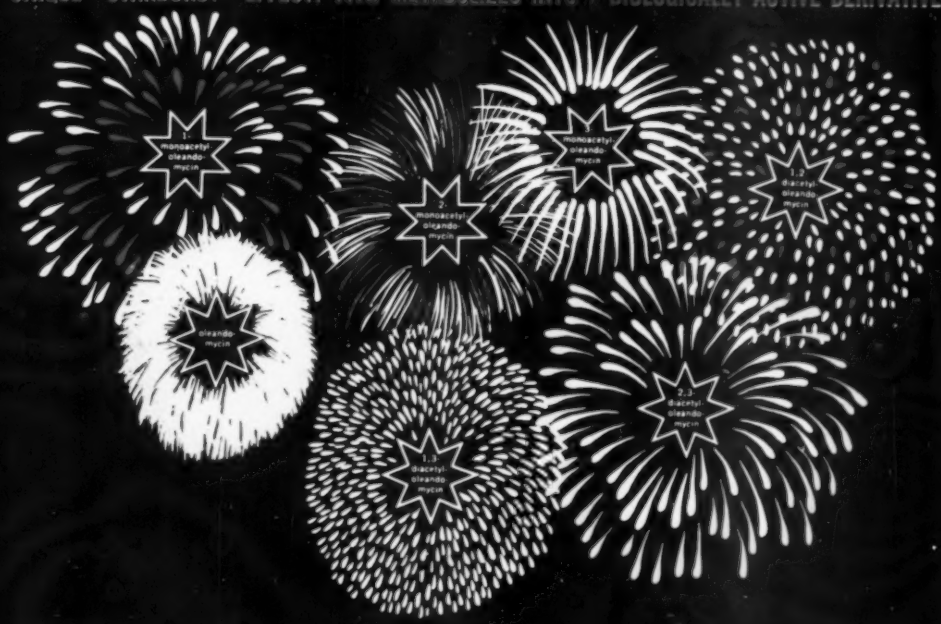

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1. English, A. R., and McBride, T. J.: Proc. Soc. Exper. Biol. & Med. 100:880 (Apr.) 1959. 2. Celmer, W. D.: Antibiotics Annual 1958-1959, New York, Medical Encyclopedia, Inc., 1959, p. 277. 3. English, A. R., and Fink, F. C.: Antibiotics & Chemother. 8:420 (Aug.) 1958.

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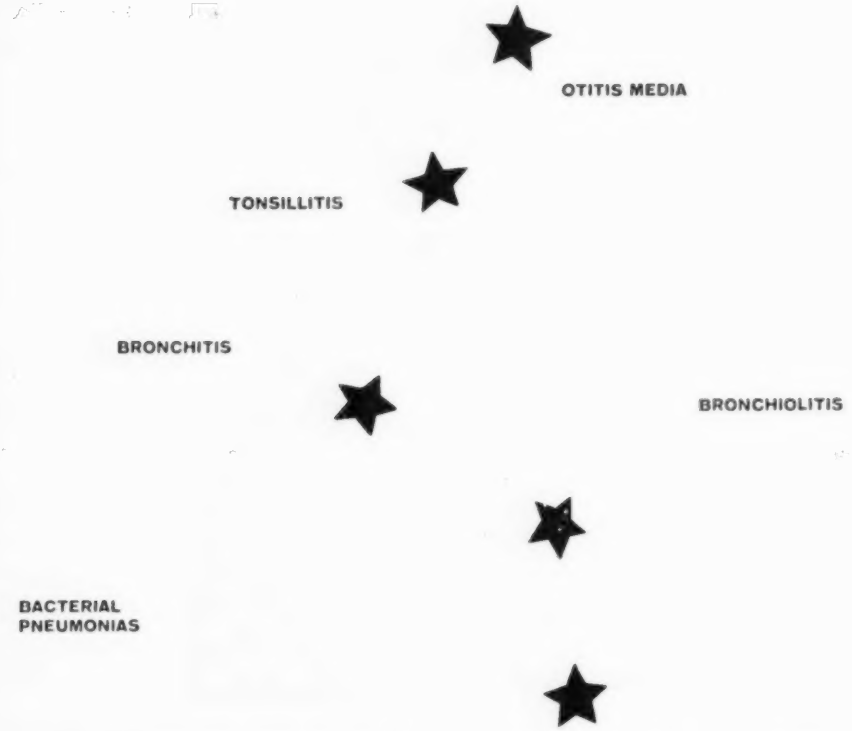

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1. Lysaught, J. N., and Cleaver, W.: Proceedings of the Detroit Symposium on Antibacterial Therapy (Michigan and Wayne County Academies of General Practice, Detroit, Sept. 12, 1959).

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